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ARTICLE

Associations of the ages at menarche and menopause with blood pressure and hypertension among middle-aged and older Chinese women: a cross-sectional analysis of the baseline data of the China Health and Retirement Longitudinal Study

Luqi Shen[1] · Li Wang[2] · Ying Hu[3] · Tingting Liu[4] · Jinzhen Guo[5] · Ye Shen[1] · Ruiyuan Zhang[1] · Toni Miles[1] · Changwei Li[1]

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Abstract

We evaluated the associations of the ages at menarche and menopause with blood pressure (BP) and hypertension using the baseline data of 7893 women from the China Health and Retirement Longitudinal Study, a nationally representative survey among Chinese adults aged ≥45 years. Multivariate linear and logistic regression analyses were performed to evaluate the associations of the ages at menarche and men`opause with BP and hypertension, respectively. Nonlinear associations were evaluated using spline analyses. After controlling for age, education, marital status, living areas, smoking, drinking, and medication use if necessary, an early onset of menarche by 1 year was associated with a 6% (95% confidence interval [CI]: 3–9%) higher odds of hypertension and 0.82 mm Hg ($P < 0.001$) and 0.41 mm Hg ($P < 0.001$) higher systolic and diastolic BP, respectively. When further controlling for the body mass index (BMI), blood glucose, and lipids, the associations were still significant. Spline analyses did not support U-shaped relationships between menarche age and hypertension risk ($P = 0.35$), systolic BP ($P = 0.60$), or diastolic BP ($P = 0.70$). When stratified by location of residence, menarche age was only associated with BP and hypertension among women living in rural areas. The age of menopause was positively associated with hypertension (odds ratio [OR] = 1.02 per year delay of menopause, 95% CI: 1.01–1.03). However, when further controlling for BMI, such an association no longer existed (OR = 1.01, $P = 0.32$). These findings indicated that the associations of menarche age with BP and hypertension may be modified by factors related to the area of residence in China, and the association between menopause age and hypertension was driven by BMI.

Keywords Blood pressure · Hypertension · Menarche · Menopause · National survey

Introduction

Both the ages of menarche and menopause have been associated with blood pressure (BP) and/or hypertension in previous studies. Among children and adolescents, early menarche is associated with higher BP and risk for hypertension [1, 2]; however, studies on the long-term association of early menarche with hypertension among adults have

These authors contributed equally: L. Shen, L. Wang, Y. Hu

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✉ Changwei Li
changwei.li@uga.edu

[1] Department of Epidemiology & Biostatistics, University of Georgia College of Public Health, Athens, GA, USA

[2] Department of Obstetrics and Gynaecology, Shanghai Baoshan Luo Dian Hospital, Shanghai, China

[3] Department of Obstetrics and Gynaecology, West China Second University Hospital, Key Laboratory of Birth Defects and Related Diseases of Women and Children, Ministry of Education, Sichuan University, Chengdu, Sichuan Province, China

[4] School of Nursing, University of Arkansas College of Education and Health Professions, Fayetteville, AR, USA

[5] Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX, USA

yielded inconsistent findings. A study among 7119 Chinese women revealed that women with late menarche (later than 18 years old) had a 39% higher risk of developing hypertension [3]. By contrast, an even larger study among 13,242 women reported that instead of late menarche, early menarche was associated with a higher risk of self-reported hypertension [4]. Interestingly, a large-scale study among UK women demonstrated that the relationship between age at menarche and hypertension was U-shaped, with both early and late menarche showing an increased risk for hypertension [5]. It is unclear whether such a U-shaped association exists among women of Asian ancestry. Meanwhile, many studies have reported that women who live in settings with poor nutrition, such as rural areas, had an earlier age of menarche [6, 7]. It is worthwhile to explore whether living in such settings modifies the association between early menarche and hypertension risk.

Menopause is associated with increased salt sensitivity of BP [8]. Among postmenopausal women, menopausal age was reported to be inversely associated with BP and the risk of hypertension [9, 10]. Loss of estrogen was proposed to drive the development of hypertension among postmenopausal women. A study by Scuteri and colleagues demonstrated that among postmenopausal women, those taking hormone replacement therapy had less systolic BP (SBP) increase over the 10 years' follow-up than nonusers [11]. Therefore, estrogen therapy was recommended for patients with hypertension. However, estrogen loss is not the only mechanism of hypertension among postmenopausal women. The menopausal period is a time in which dramatic changes occur to both physical and mental faculties. Additionally, women at menopausal age had a higher prevalence of metabolic-related disease, such as dyslipidemia and diabetes. Lifestyle behavior and metabolic disorders may also play an important role in the development of hypertension among menopausal women.

Therefore, the aims of the current study were to investigate the association of menarche and menopause age with the risk of hypertension in late adulthood among Chinese women and to evaluate how lifestyle behaviors, metabolic disorders, and area of residence impact such associations through a cross-sectional analysis of the baseline data of the China Health and Retirement Longitudinal Study (CHARLS).

Methods

Study population and design

CHARLS is a series of biannual surveys among a nationally representative sample of Chinese adults aged 45 years and older [12]. It was designed to describe the dynamics of retirement and its impact on health, health insurance, and economic well-being in China. The first wave of data was collected between June 2011 and March 2012 by trained interviewers during a face-to-face household encounter. The data consist of comprehensive and detailed information on socioeconomic indicators, biomedical measurements, the health status, and functional indicators [12].

A detailed sampling design of CHARLS has been described in previous publications [13, 14]. Briefly, the survey used a four-stage, stratified, cluster probability sampling design [12]. The response rate among eligible households was 80.51% [15]. The response rate was higher among rural households than among urban households (94.15% vs. 68.63%) [15]. Overall, 17,708 individuals within 10,257 households were interviewed in the baseline survey [12, 15]. In total, 7893 women reported the ages at menarche and/or menopause and were included in this cross-sectional study.

Ages at menarche and menopause, reproductive years, and covariates

The ages at menarche and menopause and demographic and social economic variables, including age, sex, education level, marital status, and number of biological children, were measured by self-reporting. Reproductive years were calculated for postmenopausal women by subtracting the menarche age from the menopause age. Marital status was categorized as "married and living with spouse" and others (including "married but temporarily separated", "separated", "divorced", "widowed", and "never married"). Education levels were measured as "illiterate", "less than elementary school", "elementary school", "middle school", "high school", and "above vocational school". Drinking and smoking information was collected using a standardized questionnaire [12]. Drinking status was categorized as current drinkers, former drinker, and never drinkers. Smoking was categorized as current smokers, former smokers, and never smokers.

Body weight and height were measured with the participants in light indoor clothing using a health meter (Omron™ HN-286, Kyoto, Japan) and a stadiometer (Seca™ 213, Hamburg, Germany), respectively. The body mass index (BMI) was calculated by dividing the weight in kilograms by the square of the height in meters. Fasting blood samples were collected by trained staff from the China Center for Disease Control and Prevention (CDC). Plasma was separated from blood samples and stored at −20 °C [16], and whole blood for the glycated hemoglobin A1c (HbA1c) assay was stored immediately and during shipment at 4 °C [16]. All the blood samples were transported within 2 weeks to the China CDC where samples were placed at −80 °C in a deep freezer before assay [16]. Blood assays were performed

at the Youanmen Center for Clinical Laboratory of Capital Medical University between February 2013 and June 2013 [16]. The laboratory used quality-control samples daily during the testing of the CHARLS blood samples, and all test results were within two standard deviations (SDs) of the mean quality-control concentrations. Glucose, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides were measured using enzymatic colorimetric tests, and HbA1c was analyzed using boronate affinity chromatography [16].

Blood pressure and hypertension

BP was measured three times for each participant using an Automatic Upper Arm Blood Pressure Monitor (Omron HEM-7200) by trained staff according to the standard protocol after the participant rested for 30 min [15]. Specifically, participants were instructed to sit comfortably on a chair with both feet on the floor, left upper arm supported on a table to the level of heart, and the palm facing up. They were then asked to roll their sleeve up, unless they wore a short sleeve shirt or a thin shirt. A cuff was placed and adjusted on the upper arm, so that the bottom of the cuff was approximately half an inch above the elbow, the cuff was in direct contact with the skin, and the air tube was centered on the participants' arms. Trained staff then started the monitor and recorded the SBP and diastolic BP (DBP) three times. A stop watch was used to ensure that there were 45- to 60-s gaps between two measurements. The mean of the three measurements was calculated and used in the current analyses. Data on antihypertensive medication use were collected by the question, "Are you now taking any of the following medications to treat or control your hypertension?" Those who reported taking traditional Chinese medicine or western modern medicine to treat hypertension were defined as current users of antihypertensive medications. Hypertension was defined as currently taking antihypertensive medicine, SBP ≥ 140 mm Hg, or DBP ≥ 90 mm Hg.

Statistical analysis

Continuous variables were presented as the means (SD) or medians (interquartile range), and categorical variables were shown as percentages among the overall participants and by quartiles of ages at menarche. Continuous variables were checked for normality and were log-transformed, if necessary. Binary association analyses were conducted between the quartiles of the ages at menarche and covariates using Chi-squared test for categorical variables and one-way analysis of variance for continuous variables. The effect of age at menarche or menopause was evaluated by multivariate logistic regression models for hypertension, and multivariate linear regression models for BP. We built three sets of models. Model 1 controlled for age, education, marital status, area of residence (rural vs. urban), smoking, drinking, and antihypertensive medication use, if necessary. Model 2 additionally controlled for BMI. Model 3 controlled for all variables in model 2 plus the number of biological children, fasting glucose, HbA1c, LDL-C, HDL-C, and triglycerides. Odds ratios (ORs) and 95% confidence intervals (CIs) were presented for variables in the logistic regression models. Multicollinearity was checked among all the covariables included in the full model, and none of the variables violated the criteria (Supplementary Tables 3–5) [17].

Since using traditional Chinese medicine to treat hypertension is not common in countries other than China, and the efficacy of traditional Chinese medicine in controlling BP is not clear, we performed sensitivity analyses excluding those taking only traditional Chinese medicine to treat hypertension. Furthermore, sensitivity analysis was conducted among women not taking any antihypertensive medication to rule out the impact of antihypertensive medication.

To evaluate nonlinear relationships between menarche age and BP and prevalence of hypertension, SAS macros "lgtphcurv9" [18] and "glmcurv9" [19] were used to fit restricted cubic splines to the logistic and linear regression models, respectively. The macros allowed for controlling covariates, and performed likelihood ratio tests to assess nonlinear and linear relationships [18, 19]. The mean menarche age of 16 years was chosen as a reference, and the first and last knot values were set at the 5 and 95 percentiles of menarche age, respectively.

To evaluate whether the association of early menarche with hypertension differed between women living in rural areas and those in urban areas, we performed stratified analyses by area of residence. Interactions between the area of residence and menarche age were assessed by adding an interaction term, menarche∗living area in the models.

SAS 9.3 (SAS Institute Inc., Cary, North Carolina) was used to perform data analyses. All P values were two-sided, and $P < 0.05$ was considered significant.

Results

The characteristics of the study participants are demonstrated in Table 1. Participants were, on average, aged 58.0 years. Most of the women (79.7%) were married and living with their spouses. A substantial proportion (39.0%) of women was illiterate, and only 9.4% had a high school or above education. Smoking and drinking prevalence rates were low (6.0% and 4.3%, respectively). The participants were, on average, normally weighted with a mean BMI of 24.0 kg/m^2. The mean ages at menarche and menopause were 16.0 and 48.8 years, respectively. About one-fifth (20.9%) of the women was taking antihypertensive medication.

Table 1 Characteristics of the CHARLS participants in the 2011 baseline survey

	Overall ($n = 7893$)	Quartiles of ages at menarche				*P*
		Q1 ($n = 1877$)	Q2 ($n = 2877$)	Q3 ($n = 1240$)	Q4 ($n = 1899$)	
Age at menarche, years, mean (SD)	16.0 (2.0)	13.3 (0.8)	15.6 (0.5)	17 (0)	18.6 (0.8)	–
Age at menopause, years, mean (SD)	48.8 (4.6)	48.7 (4.3)	49 (4.5)	49.1 (4.4)	48.7 (5)	0.66
Age, years, mean (SD)	58.0 (10.0)	56.4 (10.2)	57.6 (10.2)	58.5 (9.7)	59.9 (9.5)	<0.001
Living in rural areas, *n* (%)	5957 (75.6)	1244 (66.4)	2164 (75.3)	970 (78.2)	1579 (83.4)	<0.001
Married and lived together, *n* (%)	6286 (79.7)	1497 (79.8)	2319 (80.6)	983 (79.3)	1487 (78.3)	0.29
Number of biological children, median (IQR)	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)	1 (0–2)	<0.001
Education, *n* (%)						
Illiterate	3074 (39.0)	559 (29.8)	1031 (35.8)	547 (44.1)	937 (49.4)	<0.001
Less than elementary school	1403 (17.8)	302 (16.1)	484 (16.8)	224 (18.1)	393 (20.7)	
Elementary school	1408 (17.9)	387 (20.7)	554 (19.3)	192 (15.5)	275 (14.5)	
Middle school	1263 (16.0)	351 (18.7)	537 (18.7)	181 (14.6)	194 (10.2)	
High school	491 (6.2)	167 (8.9)	186 (6.5)	66 (5.3)	72 (3.8)	
Above vocational school	250 (3.2)	108 (5.8)	85 (3)	30 (2.4)	27 (1.4)	
Smoking status, *n* (%)						
Never	7262 (92.1)	1752 (93.5)	2652 (92.2)	1124 (90.7)	1734 (91.3)	0.02
Former smoker	154 (2.0)	22 (1.2)	55 (1.9)	28 (2.3)	49 (2.6)	
Current smoker	472 (6.0)	100 (5.3)	169 (5.9)	87 (7)	116 (6.1)	
Drinking status, *n* (%)						
Never drinker	7204 (93.5)	1732 (94.1)	2633 (93.9)	1137 (93.7)	1702 (92.1)	0.01
Former drinker	167 (2.2)	27 (1.5)	53 (1.9)	26 (2.1)	61 (3.3)	
Current drinker	333 (4.3)	81 (4.4)	117 (4.2)	51 (4.2)	84 (4.5)	
Body mass index, kg/m^2, mean (SD)	24.0 (4.1)	24.6 (4.2)	24.1 (4)	24.1 (4.3)	23.4 (4)	<0.001
Glucose, mg/dl, mean (SD)	109.6 (36.2)	110.4 (36.7)	110 (36.1)	109.7 (39.3)	108 (33.9)	0.08
Glycated hemoglobin, %, mean (SD)	5.3 (0.8)	5.3 (0.8)	5.3 (0.9)	5.3 (0.8)	5.2 (0.8)	0.22
HDL cholesterol, mg/dl, mean (SD)	51.2 (14.3)	50.3 (14.3)	50.7 (14.1)	50.8 (14)	52.9 (14.7)	<0.001
LDL cholesterol, mg/dl, mean (SD)	119.8 (35.1)	118.9 (35.3)	118.7 (34.6)	121 (36.5)	121.6 (34.8)	0.01
Triglycerides, mg/dl, median (IQR)	113.3 (80.5–162.8)	117.7 (84.1–171.7)	116.8 (82.3–167.3)	110.6 (78.8–164.6)	106.2 (77.0–146.9)	<0.001
Systolic BP, mm Hg, mean (SD)	130.2 (22.2)	130.7 (21.8)	131.2 (22.4)	128.4 (21.5)	129.4 (22.7)	0.01
Diastolic BP, mm Hg, mean (SD)	75.5 (11.8)	76.4 (11.5)	76.3 (11.8)	74.9 (11.9)	74 (11.9)	<0.001
BP-lowering medication use, *n* (%)	1651 (20.9)	405 (21.6)	594 (20.7)	262 (21.1)	390 (20.5)	0.84

CHARLS China Health and Retirement Longitudinal Study, *BP* blood pressure, *HDL* high-density lipoprotein, *IQR* interquartile range, *LDL* low-density lipoprotein, *SD* standard deviation

Table 2 Associations of ages at menarche and menopause and reproductive years with blood pressure measures among all women and postmenopausal women, respectively, in the 2011 baseline survey of the CHARLS

	Model 1		Model 2		Model 3	
	Beta (SE)/OR (95% CI)	*P*	Beta (SE)/OR (95% CI)	*P*	Beta (SE)/OR (95% CI)	*P*
Per year early for menarche among all women ($n = 6514$)						
Systolic BP	0.82 (0.13)	<0.001	0.73 (0.13)	<0.001	0.68 (0.15)	<0.001
Diastolic BP	0.41 (0.07)	<0.001	0.34 (0.07)	<0.001	0.28 (0.09)	0.001
Hypertension	1.06 (1.03–1.09)	<0.001	1.04 (1.01–1.07)	0.01	1.03 (1.00–1.07)	0.07
Per year early for menarche among postmenopausal women ($n = 4285$)						
Systolic BP	0.95 (0.17)	<0.001	0.87 (0.17)	<0.001	0.83 (0.20)	<0.001
Diastolic BP	0.46 (0.09)	<0.001	0.39 (0.09)	<0.001	0.28 (0.11)	0.01
Hypertension	1.06 (1.03–1.10)	<0.001	1.04 (1.00–1.08)	0.03	1.03 (0.99–1.07)	0.16
Per year delay for menopause among postmenopausal women ($n = 4285$)						
Systolic BP	0.09 (0.07)	0.20	0.06 (0.07)	0.42	0.05 (0.08)	0.55
Diastolic BP	0.04 (0.04)	0.36	0.004 (0.04)	0.91	−0.04 (0.04)	0.36
Hypertension	1.02 (1.00–1.03)	0.01	1.01 (0.99–1.02)	0.32	1.01 (0.99–1.02)	0.56
Per year longer of reproductive years among postmenopausal women ($n = 4,285$)						
Systolic BP	0.22 (0.07)	<0.001	0.19 (0.07)	0.003	0.19 (0.08)	0.02
Diastolic BP	0.09 (0.04)	0.01	0.06 (0.04)	0.12	0.004 (0.04)	0.92
Hypertension	1.03 (1.02–1.04)	<0.001	1.02 (1.00–1.03)	0.02	1.01 (1.00–1.03)	0.09
Per year longer of reproductive years adjusting for age at menarche among postmenopausal women ($n = 4285$)						
Systolic BP	0.09 (0.07)	0.22	0.07 (0.07)	0.35	0.07 (0.09)	0.41
Diastolic BP	0.02 (0.04)	0.60	−0.003 (0.04)	0.93	−0.05 (0.05)	0.30
Hypertension	1.02 (1.01–1.04)	0.003	1.01 (1.00–1.03)	0.10	1.01 (0.99–1.03)	0.20

Model 1 for blood pressure controlled for age, education, marital status, living areas, smoking, drinking, and antihypertensive medication use

Model 1 for hypertension controlled for age, education, marital status, living areas, smoking, and drinking

Model 2 controlled for all variables in model 1 plus body mass index

Model 3 controlled for all variables in model 2 plus number of children, fasting glucose, hemoglobin A1c, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides

CHARLS China Health and Retirement Longitudinal Study, *BP* blood pressure, *CI* confidence interval, *OR* odds ratio, *SE* standard error

Association of age at menarche with BP and hypertension

Both SBP and DBP generally decreased with the quartile of age at menarche (Table 1 and Supplementary Table 1), ranging from 130.7/76.4 mm Hg in the bottom quartile to 129.4/74.0 mm Hg in the top quartile of age at menarche. Age at menarche was negatively associated with both SBP and DBP after controlling for age, education, marital status, smoking, drinking, and antihypertensive medication use (Table 2). For women with a 1-year early onset of menarche, SBP and DBP were 0.82 ($P < 0.001$) and 0.41 ($P < 0.001$) mm Hg higher, respectively. Additionally, a 1-year early onset of menarche was associated with 6% (95% CI: 3–9%; $P < 0.001$) higher odds of hypertension when adjusting for age, education, marital status, smoking, and drinking. When further controlling for BMI, number of biological children, fasting glucose, HbA1c, LDL-C, HDL-C, and triglycerides, the associations were attenuated but still significant for SBP ($\beta = 0.68$; $P < 0.001$) and DBP ($\beta = 0.28$; $P = 0.001$) and marginally significant for hypertension (OR = 1.03; $P = 0.07$). The associations of age at menarche with BP and hypertension were similar among postmenopausal women. Sensitivity analyses excluding women taking traditional Chinese medicine to treat hypertension (Table 3) or among women not taking any antihypertensive medication (Supplementary Table 2) yielded similar results. Spline analyses did not support U-shaped associations between menarche age and the odds for hypertension ($P = 0.35$), SBP (P for curve = 0.60), or DBP (P for the overall curve = 0.70) (Supplementary Figure 1–3).

When broken down by area of residence, the associations of menarche age with blood pressure and hypertension were only significant among women living in rural areas. There were significant interactions between menarche age and

Table 3 Sensitivity analyses for associations of ages at menarche and menopause with blood pressure measures excluding women taking only traditional Chinese medicine to treat hypertension, in the 2011 baseline survey of the CHARLS

	Model 1		Model 2		Model 3	
	Beta (SE)/OR (95% CI)	*P*	Beta (SE)/OR (95% CI)	*P*	Beta (SE)/OR (95% CI)	*P*
Per year early for menarche among all women ($n = 6514$)						
Systolic BP	0.80 (0.13)	<0.001	0.71 (0.13)	<0.001	0.65 (0.15)	<0.001
Diastolic BP	0.40 (0.07)	<0.001	0.33 (0.07)	<0.001	0.27 (0.09)	0.002
Hypertension	1.06 (1.03–1.09)	<0.001	1.04 (1.01–1.07)	0.01	1.03 (1.00–1.07)	0.05
Per year early for menarche among postmenopausal women ($n = 4285$)						
Systolic BP	0.93 (0.17)	<0.001	0.85 (0.17)	<0.001	0.80 (0.20)	<0.001
Diastolic BP	0.44 (0.09)	<0.001	0.36 (0.09)	<0.001	0.26 (0.11)	0.02
Hypertension	1.06 (1.03–1.10)	<0.001	1.04 (1.01–1.08)	0.02	1.03 (0.99–1.08)	0.12
Per year delay for menopause among postmenopausal women ($n = 4285$)						
Systolic BP	0.08 (0.07)	0.24	0.05 (0.07)	0.48	0.05 (0.08)	0.58
Diastolic BP	0.03 (0.04)	0.40	0.0004 (0.04)	0.99	−0.04 (0.04)	0.34
Hypertension	1.02 (1.00–1.03)	0.01	1.01 (0.99–1.02)	0.35	1.01 (0.99–1.02)	0.57

Model 1 for blood pressure controlled for age, education, marital status, living areas, smoking, drinking, and antihypertensive medication use

Model 1 for hypertension controlled for age, education, marital status, living areas, smoking, and drinking

Model 2 controlled for all variables in model 1 plus body mass index

Model 3 controlled for all variables in model 2 plus number of children, fasting glucose, hemoglobin A1c, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides

CHARLS China Health and Retirement Longitudinal Study, *BP* blood pressure, *CI* confidence interval, *OR* odds ratio, *SE* standard error

area of residence for SBP ($P = 0.02$) and DBP ($P = 0.01$) and a marginally significant interaction for hypertension ($P = 0.06$) (Table 4). After adjusting for age, education, marital status, smoking, drinking, and medication use, a 1-year early onset of menarche was associated with 1.01 mm Hg higher ($P < 0.001$) SBP among rural women, while only 0.31 mm Hg higher ($P = 0.27$) SBP among urban women. The effect sizes of a 1-year early onset of menarche were 0.52 ($P < 0.001$) and 0.08 ($P = 0.65$) mm Hg for DBP among rural and urban women, respectively. Additionally, a 1-year early onset of menarche was associated with 8% (95% CI: 4 to 11%; $P < 0.001$) and 1% (−4 to 7%; $P = 0.63$) higher odds of hypertension among rural and urban women, respectively.

Association of age at menopause with BP and hypertension

After controlling for covariates in the base model, age at menopause was positively associated with the risk of hypertension only (Table 2). Women with a 1-year later onset of menopause had a 2% (95% CI: 0–3%, $P = 0.01$) higher odds of hypertension. However, when further controlling for BMI, age at menopause was no longer associated with hypertension (OR = 1.01; $P = 0.30$). Sensitivity analyses excluding women only taking traditional Chinese medicine to treat hypertension showed similar results (Table 3). Sensitivity analyses excluding women taking antihypertensive medicine yielded similar results (Supplementary Table 2).

Association of reproductive years with BP and hypertension

Age, education, marital status, location of residence, smoking, drinking, and antihypertensive medication adjusted analyses showed that per year longer of reproductive time was associated with 0.22 mm Hg ($P < 0.001$) higher SBP, 0.09 mm Hg ($P = 0.01$) higher DBP, and 1.03 (95% CI: 1.02–1.04) times higher odds of having hypertension (Table 2). However, when further adjusting for age at menarche, reproductive years were not associated with SBP ($P = 0.22$) or DBP ($P = 0.60$). The association of reproductive age with hypertension was driven by age at menarche and postmenopausal BMI. When additionally controlling for the two variables, reproductive years were not associated with hypertension (OR = 1.01; $P = 0.10$).

Discussion

Among a nationally representative sample of middle-aged and older women in China, we identified that the early onset of menarche was significantly associated with increased BP

Table 4 Associations between ages at menarche and blood pressure measures at middle and older age by living areas in the 2011 baseline survey of the CHARLS

	Model 1		P_{int}	Model 2		P_{int}	Model 3		P_{int}
	Beta (SE)/OR (95% CI	*P*		Beta (SE)/OR (95% CI	*P*		Beta (SE)/OR (95% CI	*P*	
Systolic BP									
Rural ($n = 5130$)	1.01 (0.15)	<0.001	0.02	0.85 (0.15)	<0.001	0.03	0.79 (0.18)	<0.001	0.07
Urban ($n = 1377$)	0.31 (0.29)	0.27		0.19 (0.28)	0.50		0.08 (0.35)	0.82	
Diastolic BP									
Rural ($n = 5132$)	0.52 (0.09)	<0.001	0.01	0.42 (0.08)	<0.001	0.02	0.33 (0.10)	0.001	0.12
Urban ($n = 1377$)	0.08 (0.17)	0.65		0.01 (0.16)	0.96		0.01 (0.20)	0.97	
Hypertension									
Rural ($n = 5289$)	1.08 (1.04–1.11)	<0.001	0.06	1.05 (1.02–1.09)	0.002	0.04	1.04 (1.01–1.08)	0.02	0.14
Urban ($n = 1505$)	1.01 (0.96–1.07)	0.63		0.98 (0.92–1.04)	0.40		0.98 (0.91–1.06)	0.37	

Model 1 for blood pressure controlled for age, education, marital status, smoking, drinking, and antihypertensive medication use

Model 1 for hypertension controlled for age, education, marital status, smoking, and drinking

Model 2 controlled for all variables in model 1 plus body mass index

Model 3 controlled for all variables in model 2 plus number of children, fasting glucose, hemoglobin A1c, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglycerides

CHARLS China Health and Retirement Longitudinal Study, *BP* blood pressure, *CI* confidence interval, *OR* odds ratio, *SE* standard error, P_{int} *P* value from the interaction test

and the risk of hypertension in late adulthood independent of social economic factors, lifestyle behavior, and metabolic measures. Menopause age was positively associated with the risk of hypertension; however, the association was dependent on BMI. Our findings provide robust evidence for a long-term association between early menarche and BP regulation and suggest that weight management may help to prevent hypertension among postmenopausal women.

Early menarche was associated with higher BP and higher odds of hypertension in the current study. These findings are consistent with those of a previous meta-analyses among adult women aged 20 years or older, in which early menarche was associated with a 25% higher odds of having hypertension [20]. Our study contributes further evidence that early menarche increases both BP and the odds of hypertension among a middle-aged and older female Chinese population. A recent study among 6252 postmenopausal Chinese women recruited in Henan province, China reported that women with older age at menarche had a higher prevalence of hypertension, but the association was not statistically significant [21]. However, the study participants were much older than those in CHARLS and information on antihypertensive medication use was not included in the definition of hypertension [21].

Our data did not support a U-shaped association between menarche age and hypertension. One possible reason is that CHARLS participants had late menarche compared with those in the UK Million Study, in which a U-shaped association between age at menarche and hypertension was identified. The UK Million Study participants had an average age at menarche of 13.0 years (SD = 1.6 years; interquartile range: 12–14 years), and the turning point for the U-shaped association was 13 years. The mean age at menarche in our study was 16 years (SD = 2 years; interquartile range: 13–19 years). Thus, age at menarche in the current study was systematically deviated to the right of the turning age point as described in the UK Million Study, and we could not detect such a relationship. Other possible reasons contributing to the discrepancy include different genetic backgrounds, birth weight, and lifestyle behaviors between the two study populations [22, 23]. Further studies are warranted to explore the mechanisms underlying the difference.

The average age at menarche in our population was much delayed compared with that of other populations. This may have reflected early-life malnutrition in this population. A previous study from our group revealed that more than 11.6% of the middle-aged and older Chinese adults had their family member(s) starved to death during the Chinese great famine in 1959–1961, and the proportion was even higher in rural areas [24]. It is possible that poor nutrition in early life may have delayed menarche in the current study population and subsequently exerted a risk for hypertension in late life. Therefore, late onset of menarche can be a proxy for early-life malnutrition or a mediator through which early-life malnutrition exerts a risk for hypertension. Future studies exploring the relationship between the Chinese great famine, age at menarche, and risk for hypertension in late life may help to delineate their relationships.

Furthermore, our study revealed that the association of early menarche with hypertension was only significant among women living in rural areas but not among those living in urban areas. Area of residence is a proxy for many factors in China. Women living in urban areas have access to better health care facilities, sufficient nutrition, and a less stressful lifestyle. These factors may have helped alleviate the impact of early menarche on risk for hypertension among women living in urban areas. Future studies focusing on factors mediating the early menarche and hypertension association will help to delineate the mechanism underlying hypertension and reduce the hypertension burden among middle-aged and older women.

In the current study, age of menopause was positively associated with the odds of hypertension, and this association was dependent on BMI. Inconsistent associations between age at menopause and hypertension have been reported from previous studies [9, 10, 25]. A small study among 150 postmenopausal women reported an inverse association between menopause age and BP [10]; however, BMI was not considered in the study. A recent study among 13,406 postmenopausal women also reported that women with a 1-year delay in menopause had a 2% lower prevalence of hypertension [9]. Similar to our findings, in the Japanese Nurse's Health Study, Lee et al. reported a positive association between age at menopause and hypertension; however, the association disappeared after adjusting for BMI [25]. Participants in our study were, on average, 5–9 years younger than those in the first two studies, and participants in the Japanese Nurse's Health Study were even younger than those in our study. It is possible that our findings were more relevant to women shortly after menopause. Furthermore, our study revealed that BMI mediated the association between age at menopause and hypertension. Obesity is an important risk factor for hypertension [26–28]. Women around menopause had increased body weight due to the transition of hormone and metabolism levels [29]. The prevalence of obesity among postmenopausal women can be as high as 40% [30]. Our study contributed further knowledge that women at menopause age should closely monitor their body weight to prevent hypertension.

Our study has important strengths. First, we used data from a nationally representative survey. Therefore, the findings from our study are generalizable to all middle-aged and older women in China. Second, strict quality-control measures, including Global Positioning System (GPS) matching, data checking, recording and checking interviews, and calling back participants, were implemented at every stage of the study to ensure data quality and reliability. Our study also had limitations. First, our study focused on middle-aged and older women only, and the effect of menarche age on younger women cannot be evaluated. Second, our study was a cross-sectional analysis. Although we are certain that menarche occurs before hypertension events and the temporal relationship between age at menarche and hypertension is clear, the time sequence of hypertension and menopause was unclear. Additionally, the incidence-prevalence bias cannot be fully ruled out. Since hypertension is an important risk factor for cardiovascular disease and mortality, it is possible that the existing hypertensive participants were those with less severe hypertension and could survive to the survey. Future longitudinal analyses are warranted to confirm our study findings. Finally, self-reported ages at menarche and age of menopause have been used in the current study. This may cause recall bias, particularly for age at menarche. In addition, irregular menstruation before menopause may also introduce recall bias. However, previous studies have shown that self-reporting is a valid method to measure the ages at menarche and menopause among middle-aged and older women [31, 32], and this method has been widely used in large-scale population-based epidemiologic studies on menarche and/or menopause [4, 25, 33].

To conclude, we identified that early menarche increased the risk for hypertension in middle-aged and older Chinese women. Such an association was more prominent among women living in rural areas. In addition, BMI mediated the association between menopause age and the risk of hypertension. Controlling body weight may help women at the menopause stage to prevent hypertension.

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Compliance with ethical standards

Conflict of interest: The authors declare that they have no conflict of interest.

Ethics approval: The CHARLS study data are publicly available and are open to researchers all over the world. The current study is a secondary analysis of the deidentified CHARLS study data. The Institutional Review Boards at the University of Georgia granted the current study exemption from review.

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