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High waist circumference is a risk factor of new-onset hypertension: Evidence from the China Health and Retirement Longitudinal Study

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Abstract

This study aims to investigate the association between waist circumference and the development of hypertension based on a nationwide cohort Chinese population. A total of 5330 individuals free of hypertension at baseline were collected from the China Health and Retirement Longitudinal Study. The association between waist circumference and the development of hypertension was analyzed by an adjusted cox regression model and visualized by restricted cubic splines. Further, we applied the supervised machine learning methods to evaluate the importance of multiple variates for newonset hypertension. Additionally, the robustness of the association was assessed by a subgroup analysis. A total of 1490 individuals (28.0%) developed hypertension during a mean follow-up of 3.32 years. The new-onset hypertension was more observed in those with increased waist circumference (P for trend < .001). In the fully adjusted Cox regression, each 10 cm increase of waist circumference would result in an 18% elevated risk of hypertension. The random forest method and the Extreme Gradient Boosting method revealed waist circumference as an important feature to predict the development of hypertension. The sensitivity analysis indicated a consistent trend between waist circumference and new-onset hypertension in all BMI categories. This study suggested high waist circumference as an independent risk factor for new-onset hypertension based on a nationwide cohort of Chinese adults aged ≥45 years old. Our results supported that waist circumference should be routinely measured.

KEYWORDS

body mass index, hypertension, normal-weight obesity, waist circumference

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1 | INTRODUCTION

Due to population aging and unfavorable health behaviors,¹ hypertension has become a significant health problem with increasing trend, which contributes to about 50% morbidity and 20% mortality related to cardiovascular diseases in China.^{2–5} Among the many risk factors, obesity is a chronic metabolic disorder closely associated with hypertension. Despite the increase in obesity prevalence, mortality caused by coronary artery disease and stroke has declined over the last decade, probably owing to the improved public health management on other cardiovascular risk factors.⁶ However, the prevalence of hypertension shows a consistently increasing trend.⁷

Body mass index (BMI) remains the most widely used measure to monitor obesity and assess the related cardiovascular risk. However, the BMI-defined obesity is a heterogeneous condition at the individual level since BMI fails to capture the regional body fat distribution.⁸ Individuals with mildly higher BMI are associated with better survival and fewer cardiovascular events, which was termed as the "obesity paradox." Compared with BMI, waist circumference is another anthropometric measure strongly associated with the absolute abdominal fat distribution.⁹ A recent consensus statement highlighted that waist circumference could provide incremental information to the clinician beyond BMI. Also, the influence of waist circumference on cardiovascular risk could be fully revealed only when BMI was adjusted for.^{10–12}

More in-depth insight on the association between waist circumference and hypertension is the key to better managing abdominal obesity-related cardiometabolic risk, which provides additional opportunities for the primary prevention of cardiovascular diseases.¹³ Our recent publications have revealed the significant association between waist circumference and the prevalence of hypertension,^{14,15} consistent with the evidence from other research groups.^{16,17} However, most of the previous studies were cross-sectional based on Western populations.

Therefore, this study aims to investigate the association between waist circumference and the development of hypertension based on a nationwide cohort Chinese population.

2 | METHODS

2.1 Data source and study population

The China Health and Retirement Longitudinal Study (CHARLS) is an ongoing survey that enrolls a nationally representative sample of the Chinese population aged 45 or older from 150 counties/districts and 450 villages/resident committees. CHARLS study collected information on social demographics, health status and functioning, anthropometric measurement, and blood tests. A detailed study design of CHARLS has been previously documented.¹⁸ The baseline national wave (first wave) was conducted in 2011, and the enrolled individuals were followed up every 2 years. This study analyzed the baseline wave (in 2011) and two follow-ups (second wave in 2013 and third wave in 2015) of CHARLS.

Figure 1 shows the flow chart of the selection of eligible participants. We included the individuals with at least a follow-up record in this study. The exclusion criteria were as follows (1) participants without blood pressure measure; (2) diagnosed with cancer or malignant tumor; (3) missing BMI or waist circumference records; (4) diagnosed with hypertension in the baseline wave. Finally, a total of 5330 participants without baseline hypertension were enrolled in this study. The Ethics Review Committee of Peking University approved the CHARLS study (IRB00001052-11015), and written informed consent was obtained from all participants before involvement.

2.2 | Waist circumference measurement

After the participant was kept in a standing position, a trained examiner would locate the belly button and then place a soft measuring tape around the waist at the navel level. Next, the participant would be asked to take a normal breath and hold a breath at the end of exhaling. Then, waist circumference was measured after the participant exhaled one normal breath. A detailed description of waist circumference measurement was provided in the CHARLS Biomarker Questionnaire Protocol (http://charls.pku.edu.cn/pages/data/2011-charls-wave1/zh-cn. html).

2.3 | Hypertension definition

After resting about 30 min in a seated position, the lower edge of the cuff was placed about .5 inches above the elbow. Systolic and diastolic blood pressure was measured three times by one trained examiner using an automatic blood pressure monitor (Omron HEM-7200 Monitor). The average blood pressure was calculated accordingly. In this study, the individual satisfying one of the following three criteria was identified as hypertension: (1) average systolic blood pressure \geq 140 mmHg or diastolic blood pressure \geq 90 mmHg¹⁹; (2) self-reported hypertension; (3) current administration of antihypertensive medications.^{14,20,21}

2.4 | Covariates

Demographic information, metabolic biomarkers, medical history, and health behavioral factors were included as covariates to control the related bias. Demographic information (age and gender), medical history (self-reported diabetes, heart disease, and stroke), and health behaviors (smoking status and alcohol consumption) were obtained from face-to-face household interviews using structured questionnaires. After household interviews, 8 ml fasting venous blood was collected by trained staff. The blood samples were transported to the Chinese Center for Disease Control and Prevention laboratory in Beijing and stored at -80°C.¹⁸ Metabolic biomarkers were acquired following a standard protocol, including triglycerides, low-density lipoprotein, total cholesterol, creatinine, fasting plasma glucose, and hemoglobin



FIGURE 1 Flow chart of selection of eligible participants from the China Health and Retirement Longitudinal Study. BMI: body mass index

A1c (HbA1c). The estimated glomerular filtration rate (eGFR) was acquired using the Chronic Kidney Disease-Epidemiology Collaboration equation.²² BMI was calculated as $\frac{Weight (kg)}{Height^2 (m^2)}$.

Additionally, diabetes was defined as (1) fasting plasma glucose \geq 126 mg/dl; (2) HbA1c \geq 6.5%; or (3) self-reported diabetes in this study. Heart disease was acquired by the following question "Have you been diagnosed with heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems by a doctor? (Yes/No)." Stroke was acquired by the following question "Have you been diagnosed with Stroke by a doctor? (Yes/No)." Detailed protocols for questionnaires and laboratory examination were provided on the CHARLS website.

2.5 | Statistical analysis

We performed statistical analyses according to the recommendation of the American Heart Association Scientific Publication Committee.²³ The missing covariates were filled by multivariate multiple imputation method to reduce selection bias and enhance statistical power.^{24,25} We reported normally distributed variables (decided by Kolmogorov-Smirnov test) as mean \pm standard deviation, and the skewed distributed ones were represented as median with interquartile range. Categorical variables were provided as frequencies with percentages. The baseline characteristics were compared among waist circumference quartiles by one way ANOVA test (normal distribution), Kruskal-Wall is test (skewed distribution), or chi-square test (categorical variables). Also, the generalized additive model and Spearman correlation analysis were used to evaluate the association between waist circumference and the baseline systolic/diastolic blood pressure. We used Cox regression analysis to evaluate the association between waist circumference and the development of hypertension, and the hazard ratio (HRs) with 95% confidence intervals (CIs) were calculated. In the minimally adjusted model, we adjusted for age, gender, low-density lipoprotein, diabetes, heart disease, stroke, the administration of antidiabetic medications, smoking status, and alcohol consumption. BMI was additionally adjusted for in the fully adjusted model. Moreover, we illustrated the influence of waist circumference on newonset hypertension via a restricted cubic spline (RCS) with four knots located at the 5th, 35th, 65th, and 95th percentiles. RCS were performed in males and females, respectively, and the median waist circumference (82.0 cm for males and 83 cm for females) was set as the reference.²⁶

Machining learning methods could mathematically and accurately fit data without linear assumptions. In this study, we applied the random forest machine learning method to evaluate the variate importance for the future development of hypertension, including waist circumference, BMI, age, gender, total cholesterol, LDL, triglycerides, eGFR, fasting plasma glucose, HbA1c, CRP, diabetes, heart diseases, stroke, dyslipidemia, smoking status, alcohol consumption. The random forest method quantifies the variable importance contributing to new-onset hypertension by mean decrease accuracy, a higher value of which indicates a significant weight. Besides, the eXtreme Gradient Boosting (XGBoost) was also used to assess the variate importance. XGBoost is a novel ensemble learning algorithm based on the boosted decision tree, which generally showed superior performance than other machine learning methods. Higher variable importance indicates a more contributing role in the development of hypertension.

Moreover, we performed a sensitivity analysis of cox regression in different subgroups, including BMI categories (<24 kg/m², 24–

28 kg/m², and >28 kg/m²), gender (male or female), age (<60 or \geq 60 years), and eGFR (below median, or equal or above median). P < .05 was considered statistically significant. Additionally, we also analyzed the association using the cut-off value of 130/80 mmHg for hypertension.²⁷ All statistical analyses were performed using R software (version 4.1.1).

RESULTS 3

3.1 Characteristics of the study population

Table 1 summarizes the characteristics of all participants according to waist circumference quartiles. The study cohort consisted of 5330 individuals with a mean age of 57.4 years old, and 47.3% of them were males. The age-adjusted mean waist circumference was 83.0 cm in males and 83.4 cm in females. In the baseline wave, although all 5330 participants were without hypertension, the systolic and diastolic blood pressure elevated with the increasing waist circumference (Figure 2A,B). Consistently, spearman's rank revealed the positive correlation of waist circumference with systolic (correlation coefficient = .17, P < .001) and diastolic blood pressure (correlation coefficient = .19, P < .001). Compared with the low waist circumference group, individuals with high waist circumference had increased triglycerides, LDL, fasting plasma glucose, and more were diagnosed with diabetes or heart disease. However, no significant difference was observed in creatinine levels, eGFR levels, alcohol consumption, and the prevalence of stroke. Moreover, we provided patients' characteristics in the baseline, second and third wave (Supplement Table S1). Additionally, we also presented the blood pressure, waist circumference. and the percentage of hypertensives patients for each quartile (Q1-Q4) in Supplement Table S2.

3.2 Association of waist circumference with hypertension

A total of 1490 individuals (28.0%) developed hypertension during a mean follow-up of 3.32 years. The new-onset hypertension was more frequently observed in those with increased waist circumference (P for trend < .001). Table 2 summarizes the association between waist circumference and new-onset hypertension. When analyzed as a continuous variable, waist circumference significantly contributed to the development of hypertension in all three models with HRs of 1.27 (1.20-1.33), 1.27 (1.21-1.34), and 1.18 (1.09-1.28), respectively. Consistently, when we analyzed waist circumference as categories, the risk of new-onset hypertension increased with the elevated categories from Q1 to Q4. In the fully adjusted model, individuals in the fourth waist circumference quartile (Q4) exhibited a 1.35-fold risk of future hypertension when setting the lowest quartile (Q1) as reference. Restricted cubic spline regression analysis revealed a linear relationship between waist circumference and the risk of incident hyper-

tension in both males (P for non-linear = .65) and females (P for nonlinear = .12) (Figure 2C,D).

Figure 2E illustrates the variable importance related to the incident hypertension, quantified by the random forest method. Among the many variables, waist circumference showed a mean decrease accuracy of 21.3, which indicated that waist circumference is the most important factor for hypertension development, only second to age (mean decrease accuracy = 22.5). Also, the variable importance evaluated by XGBoost was summarized in Figure 2F. Consistent with random forest, XGBoost showed that waist circumference played an important role in predicting the development of hypertension.

3.3 | Sensitivity analysis

Figure 3 shows a consistent trend between waist circumference and new-onset hypertension in different subgroups, including BMI categories, gender (male or female), age (<60 or \geq 60 years), and eGFR (below the median, or equal or above median). Importantly, although a consistent trend remained, no statistically significant association was observed between waist circumference and new-onset hypertension in the subgroup of BMI > 28 kg/m^2 (HR, 1.17; 95% CI, 96–1.44; P = .128). When the cut-off value was set as 130/80 mmHg, the adjusted OR (95% CI) for waist circumference was 1.18 (1.08-1.28), similar to the cut-off value of 140/90 mmHg (Supplement Table S3).

DISCUSSION 4

BMI is a convenient anthropometric index to monitor obesity at a population level, which shows a dose-dependent relationship between multiple adverse events. However, obesity is a heterogeneous metabolic condition, where the excess visceral or ectopic fat distribution contributes to a higher metabolic and cardiovascular risk. A J- or U-shaped curve was observed between waist circumference and mortality.^{28,29} In a meta-analysis on 250,152 patients with coronary artery disease, patients with mildly elevated BMI (25-29.9 kg/m²) showed the lowest risk for all-cause mortality (relative risk, .87; 95% CI, .81-.94) and cardiovascular mortality (relative risk, .88; 95% CI, .75-1.02) than other BMI categories.³⁰ Similar results were also reported in the following analysis on general populations.³¹⁻³³

Interestingly, when BMI and waist circumference were analyzed in the same regression model, waist circumference was a risk factor for cardiovascular diseases. In contrast, BMI was instead identified as a protective or neural factor.^{10,34-38} Therefore, concerns were raised regarding the application of BMI in obesity classification since it shows poor power to evaluate the distribution of fat deposits and distinguish lean mass from body fat.^{39,40} It is proposed that the limitations of BMI in evaluating fat distribution might be a possible explanation for the obesity paradox.⁴¹

Accumulating studies have revealed the superiority of waist circumference in assessing the risk profiles related to abdominal fat distribution,⁴²⁻⁴⁴ which contributes to the introduction of waist

	Q1 [60.8, 76.2]	Q2 (76.2, 82.4]	Q3 (82.4, 89.2]	Q4 (89.2, 128]	Р
Z	1333	1336	1356	1305	
Age (year)	57.00 (50.00, 64.00)	57.00 (50.00, 63.00)	57.00 (49.00, 62.00)	56.00 (50.00, 63.00)	.008
Gender (female, %)	687 (51.54%)	654 (48.95%)	741 (54.65%)	728 (55.79%)	.002
New-onset hypertension $(n, \%)$	309 (23.18%)	329 (24.63%)	385 (28.39%)	467 (35.79%)	<.001
Waist circumference (cm)	73.00 (70.00, 75.00)	79.30 (78.00, 81.00)	86.00 (84.00, 87.50)	94.00 (91.30, 98.00)	000
BMI (kg/m ²)	19.66 (18.42, 20.90)	21.61 (20.31, 22.82)	23.41 (22.12, 24.81)	26.18 (24.47, 28.09)	000.
SBP (mmHg)	116.00 (107.33, 125.67)	117.67 (108.67, 126.42)	118.33 (110.33, 127.00)	122.33 (114.33, 129.67)	<.001
DBP (mmHg)	68.33 (62.00, 75.33)	69.67 (63.33, 75.67)	70.33 (64.67, 76.67)	73.33 (67.67, 79.00)	<.001
LDL (mg/dl)	110.18 (91.62, 129.90)	108.63 (88.14, 129.22)	114.82 (93.56, 138.11)	116.37 (95.10, 137.24)	<.001
Triglycerides (mg/dl)	81.42 (62.84, 116.82)	90.27 (66.38, 127.44)	102.22 (72.57, 144.26)	119.47 (84.08, 179.66)	<.001
Creatinine (mg/dl)	.75 (.64, .88)	.75 (.64, .87)	.75 (.63, .87)	.75 (.64, .87)	.800
eGFR (ml/min/1.73 m^2)	95.99 (86.53, 103.25)	96.44 (86.60, 103.49)	96.44 (86.69, 103.97)	96.19 (86.12, 103.07)	.530
FPG (mg/dl)	98.28 (91.44, 107.28)	100.26 (92.88, 108.36)	100.98 (93.42, 110.34)	103.32 (95.40, 114.66)	<.001
HbA1c (%)	5.10 (4.80, 5.30)	5.10 (4.80, 5.40)	5.10 (4.88, 5.40)	5.20 (4.90, 5.50)	<.001
Smoking (yes, %)	572 (42.91%)	570 (42.66%)	501 (36.95%)	443 (33.95%)	<.001
Drinking (%)					.099
More than once a month	320 (24.01%)	376 (28.14%)	341 (25.15%)	308 (23.60%)	
Less than once a month	120 (9.00%)	110(8.23%)	120 (8.85%)	102 (7.82%)	
Never	893 (66.99%)	850 (63.62%)	895 (66.00%)	895 (68.58%)	
Diabetes (yes, %)	94 (7.05%)	120 (8.98%)	156 (11.50%)	202 (15.48%)	<.001
Heart disease (yes, %)	100 (7.50%)	95 (7.11%)	106 (7.82%)	131 (10.04%)	.028
Stroke (yes, %)	12 (.90%)	11(.82%)	11 (.81%)	21 (1.61%)	.127
Abbreviations: BMI, body mass index; SBP, s HbA1c, hemoglobin A1c.	ystolic blood pressure; DBP, diast	lic blood pressure; LDL, low-density lip	ooprotein; eGFR, estimated glomerula	r filtration rate; FPG, fasting plasma glu	ucose; HbA1c:

 TABLE 1
 Baseline characteristics of enrolled individuals

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FIGURE 2 The association between waist circumference and hypertension. The fitted curve on the relationship of waist circumference with (A) systolic blood pressure and (B) diastolic blood pressure by generalized additive model. The adjusted cubic spline model on the association between waist circumference and the risk of new-onset hypertension in (C) males and (D) females based on Cox regression, respectively. BMI, age, diabetes, the administration of antidiabetic medications, smoking status, and alcohol consumption were adjusted for in the model. Median waist circumference (82.0 cm for males and 83 cm for females) was set as the reference. The variable importance is evaluated by (E) random forest and (F) eXtreme Gradient Boosting machine learning method. Higher variable importance indicates a more important role of the variable in developing hypertension. BMI, body mass index; LDL, low-density lipoprotein; FPG, fasting plasma glucose; HbA1c, hemoglobin A1c; eGFR, estimated glomerular filtration rate; CPR, c-reactive protein

TABLE 2 The association between waist circumference and risk of new-onset hypertension

	Crude model		Minimally adjusted model		Fully adjusted model	
	Hazard ratio	Р	Hazard ratio	Р	Odds ratio	Р
Waist circumference (Per 10 cm)	1.27 [1.20, 1.33]	<.001	1.27 [1.21, 1.34]	<.001	1.18 [1.09, 1.28]	<.001
Categories						
Q1 [60.8, 76.2]	Reference		Reference		Reference	
Q2 (76.2, 82.4]	1.08 [.92, 1.26]	.331	1.08 [.93, 1.27]	.302	1.02 [.87, 1.19]	.831
Q3 (82.4, 89.2]	1.27 [1.09, 1.48]	.002	1.31 [1.12, 1.52]	.001	1.15 [.98, 1.36]	.095
Q4 (89.2, 128]	1.67 [1.44, 1.93]	<.001	1.70 [1.47, 1.97]	<.001	1.35 [1.12, 1.63]	.002

Note: Crude model: nonadjusted model.

Minimally adjusted model: We adjusted for age, gender, low-density lipoprotein, diabetes, heart disease, stroke, the administration of antidiabetic medications, smoking status, and alcohol consumption.

Fully adjusted model: We adjusted for body mass index, age, gender, low-density lipoprotein, diabetes, heart disease, stroke, the administration of antidiabetic medications, smoking status, and alcohol consumption.



FIGURE 3 Sensitivity analysis on the association between waist circumference and hypertension based on cox regression analysis. The association was adjusted for BMI, age, gender (not in the gender subgroup), diabetes, smoking status, and alcohol consumption. HR, hazard ratio; CI, confidence interval; BMI, body mass index

circumference in public health. Our recent cross-sectional studies demonstrated that high waist circumference could elevate the prevalence of hypertension based on nationally representative US samples from the National Health and Nutrition Examination Survey.^{14,15} In the US individuals, waist circumference was significantly associated with (pre) hypertension with adjusted odds ratios (95% CI) of 1.28 (1.18–1.40) in the young group and 1.23 (1.15–1.33) in the old group. However, the inherent nature of cross-sectional design made it difficult to determine the causality between high waist circumference and the development of hypertension. Also, given the distinct genetic variation, disease spectrum, lifestyles, and risk factors between ethnicities, it is unclear whether the association could be fully applicable for the Chinese population.¹ As an extension of previous work, this study included 5330 participants without baseline hypertension from a nationally representative sample of the Chinese population aged \geq 45 years old. Over a mean follow-up of 3.32 years, a total of 1490 cases of incident hypertension was observed. We revealed high waist circumference as an independent risk factor for the development of hypertension (HR, 1.18; 95% Cl, 1.09–1.28).

The current guideline recommends measuring waist circumference in overweight or obese individuals.⁴⁵ Our study showed a consistent trend between waist circumference and new-onset hypertension in all

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BMI categories (<24 kg/m², 24–28 kg/m², and \geq 28 kg/m²). Interestingly, despite the consistent trend, no statistically significant association was observed in the subgroup of BMI > 28 kg/m². Together with our previous results,^{14,15} this study supported measuring and managing waist circumference regardless of BMI, which could provide additional opportunities to prevent obesity-related cardiovascular events.

Despite the strength in a nationally representative sample, rigorous study protocol, and standard statistical analysis, some limitations should be mentioned for cautious interpretation. First, although multiple confounding factors were adjusted for, potential residual covariates might remain (such as a family history of hypertension, insulin resistance, urine albumin, thyroid diseases, physical activity, diet pattern, pharmacological therapies, and so forth). Second, this study could not differentiate primary and secondary hypertension. The potential impact of waist circumference on different hypertension subtypes should be further investigated. Third, the alterations of waist circumference during follow-up were not analyzed, which might provide additional information for the development of hypertension. Fourth, this study was based on Chinese people aged ≥45 years old. It is uncertain whether the association could apply to young individuals. Moreover, a follow-up of 4 years might be insufficient to analyze the incident hypertension, and a more prolonged follow-up wave should be considered in further research. Additionally, a weak correlation was observed between waist circumference and office systolic/diastolic blood pressure despite the statistical significance. The correlation evaluated by Spearman's rank might be insufficient since it provided a crude estimation on the correlation without considering other covariates, such as BMI, age, gender, and so forth. Further study should analyze the association between waist circumference and ambulatory blood pressure via an adjusted linear regression model.

5 | CONCLUSION

This study suggested high waist circumference as an independent risk factor for new-onset hypertension based on a nationwide cohort of Chinese adults aged \geq 45 years old. Our results supported that waist circumference should be routinely measured.

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CONFLICTS OF INTEREST

The authors declared no conflict of interest.

AUTHOR CONTRIBUTIONS

Jin-Yu Sun, Qiang Qu, Xiang-Qing Kong, Wei Sun: conception and design. Xiang-Qing Kong, Wei Sun, Wen-Jun Huang: administrative

support. Jin-Yu Sun, Yong-Xiang Ma, Heng-Li Liu: data analysis and interpretation. Jin-Yu Sun, Qiang Qu, Chen Cheng: manuscript writing. All authors: final approval of manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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