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Waist circumference and incidence of hypertension in Chinese adults

Observations from the Kailuan Study

Waist circumference (WC) has been shown to be, independent of body mass index (BMI), associated with an increased risk of multiple chronic non-communicable diseases (NCDs, such as hypertension, stroke, heart disease, and diabetes mellitus) [1–6]. However, as an index of central obesity, WC has not yet been included in the final recommendations for diagnostic criteria or disease classifications by the World Health Organization [7]. Studies have considered the variations in WC by age, sex, and ethnicity, and the levels at which WC predicted the risk of different NCDs or total mortality. In fact, WC appears to increase the risk of obesity-related complications in a graded fashion rather than only at high WC thresholds.

Previous studies mainly focused on the predictive value of high WC in the risk of obesity-related chronic diseases [8–12]. A number of expert groups have attempted to develop unifying criteria for high WC in diagnosing central obesity, but they appear to be ineffective. Taking the Chinese population as an example, the consensus statement of metabolic syndrome definition at the International Diabetes Federation workshop [13] suggested abdominal obesity based on sex-specific criteria for high WC were over 80 cm and over 90 cm for Chinese women

and men, respectively. However, the Chinese Guideline for Prevention and Treatment of Patients with Hypertension recommended a WC over 85 cm for women and over 90 cm for men as the boundary values. And the results from a meta-analysis organized by the Working Group on

Obesity in China [14] showed that the cut-off points of WC for central obesity were over 80 cm and over 85 cm for Chinese women and men, respectively, in predicting obesity-related diseases.

In the present study, we examined the association between WC and the risk of

Table 1 Baseline characteristics of the study population

	Total (n = 50,024)	Male (n = 37,429)	Female (n = 12,595)
Hypertension, n (%)	22,176 (44.3)	18,301 (48.9)	3875 (30.8)
Waist circumference, cm	85.0 (9.9)	86.4 (9.3)	80.8 (10.2)
BMI, kg/m ²	24.3 (3.3)	24.5 (3.2)	23.9 (3.5)
Age, years	47.9 (12.0)	48.7 (12.3)	45.4 (10.7)
SBP, mmHg	117 (11)	118 (11)	114 (12)
DBP, mmHg	76 (7)	77 (7)	74 (7)
Resting heart rate, beats/min	72.6 (9.4)	72.6 (9.6)	72.8 (8.9)
Glucose, mmol/l	5.29 (1.44)	5.34 (1.47)	5.13 (1.33)
Total cholesterol, mmol/l	4.88 (1.08)	4.88 (1.10)	4.87 (1.02)
Triglycerides, mmol/l	1.52 (1.26)	1.59 (1.32)	1.31 (1.04)
LDL-C, mmol/l	2.30 (0.86)	2.34 (0.85)	2.18 (0.86)
HDL-C, mmol/l	1.53 (0.39)	1.51 (0.39)	1.57 (0.38)
Uric acid, μmol/l	282 (80)	297 (79)	236 (64)
Creatinine, μmol/l	88.5 (25.4)	92.0 (25.9)	78.1 (20.6)
Smoking, n (%)			
Never	29,935 (59.8)	17,569 (46.9)	12,366 (98.2)
Ever	2330 (4.7)	2292 (6.1)	38 (0.3)
Current	17,759 (35.5)	17,568 (46.9)	191 (1.5)
Alcohol consumption, n (%)			
Never	28,886 (57.7)	17,321 (46.3)	11,565 (91.8)
Ever	1484 (3.0)	1424 (3.8)	60 (0.5)
Current	19,654 (39.3)	18,684 (49.9)	970 (7.7)

Values are mean (SD) or n (%)

BMI body mass index, SBP systolic blood pressure, DBP diastolic blood pressure, LDL-C low-density lipoprotein cholesterol, HDL-C high-density lipoprotein cholesterol

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Table 2 Hazard ratios for hypertension according to waist circumference in male and female subjects

	Waist circumference groups ^a				
	Group 1	Group 2	Group 3	Group 4	Group 5
Male					
Hypertension, <i>n</i> (%)	263 (29.1)	2559 (36.0)	7670 (47.4)	5875 (57.9)	1934 (62.2)
Adjusted risk ratio (95% CI)					
Age	1	1.29 (1.14–1.47)	1.83 (1.61–2.06)	2.38 (2.10–2.69)	2.60 (2.28–2.96)
Age and BMI	1	1.16 (1.02–1.32)	1.39 (1.23–1.57)	1.56 (1.39–1.77)	1.53 (1.33–1.75)
Age, BMI, and SBP	1	1.09 (0.96–1.24)	1.24 (1.10–1.41)	1.36 (1.20–1.55)	1.34 (1.20–1.55)
Age, BMI, SBP, and DBP	1	1.08 (0.95–1.23)	1.23 (1.08–1.39)	1.33 (1.17–1.52)	1.32 (1.15–1.51)
Multivariate ^b	1	1.08 (0.95–1.23)	1.22 (1.08–1.39)	1.31 (1.15–1.49)	1.29 (1.12–1.47)
Female					
Hypertension, <i>n</i> (%)	148 (10.1)	997 (22.8)	1635 (36.8)	793 (47.5)	302 (47.6)
Adjusted risk ratio (95% CI)					
Age	1	1.81 (1.52–2.15)	2.67 (2.25–3.17)	3.50 (2.92–4.18)	3.46 (2.83–4.23)
Age and BMI	1	1.54 (1.29–1.83)	1.91 (1.60–2.28)	2.13 (1.76–2.57)	2.08 (1.68–2.58)
Age, BMI, and SBP	1	1.45 (1.21–1.72)	1.72 (1.44–2.05)	1.80 (1.49–2.18)	1.75 (1.41–2.16)
Age, BMI, SBP, and DBP	1	1.43 (1.20–1.70)	1.70 (1.43–2.03)	1.78 (1.47–2.15)	1.72 (1.39–2.12)
Multivariate ^b	1	1.43 (1.20–1.71)	1.69 (1.42–2.02)	1.76 (1.45–2.13)	1.69 (1.37–2.10)

^aWaist circumference groups: group 1, <70 cm; group 2, 70–79 cm; group 3, 80–89 cm; group 4, 90–99 cm; group 5, ≥100 cm

^bThe multivariate Cox regression model was adjusted for age, body mass index, systolic blood pressure, diastolic blood pressure, resting heart rate, glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, uric acid, creatinine, smoking, alcohol consumption

BMI body mass index, **SBP** systolic blood pressure, **DBP** diastolic blood pressure

Interaction term between waist circumference groups and sex was significant (*p* for interaction <0.001)

hypertension incidence, discussing the predictive value of low/medium/high levels of WC for hypertension in Chinese adults. Moreover, we evaluated the effects of other factors (such as BMI) on the association between WC and hypertension.

Patients and methods

Study setting and participants

All subjects were participants of the Kailuan Study (registration number: ChiCTR-TNRC-11001489) from the Kailuan community in Tangshan, a city

in the north of China. The Kailuan community is a functional and comprehensive community owned and managed by the Kailuan Group. There are 11 hospitals responsible for the health care of the community. The health records of 101,510 participants (81,110 men and 20,400 women; 18–98 years of age) from 11 hospitals during the period June 2006 to October 2007 were used. The participants met the following criteria: (1) age ≥18 years; (2) provided informed consent; and (3) updated their health status every 2 years according to the follow-up protocol. All participants completed a questionnaire and underwent clinical

examination and laboratory assessment. Standard protocols were used for all of the measurements as described earlier [15–18] and were administered by specially trained doctors and nurses. The study was performed according to the guidelines of Helsinki Declaration and was approved jointly by the Ethics Committee of the Kailuan General Hospital and Beijing Chaoyang Hospital. Written informed consent was obtained from all participants.

Until December 2013, three follow-up visits were completed for all participants. In our analysis, we excluded patients who had a history of hypertension at baseline (*n* = 45,789) and who never showed up to the three follow-up visits (*n* = 5214). After excluding those with missing values for WC (*n* = 483), a total of 50,024 participants (37,429 men and 12,595 women) were analyzed.

Data collection

Anthropometric measurements

Anthropometric indices included WC, height, and weight. All the individuals were measured wearing light clothing without shoes and hats. WC was measured to the nearest 0.1 cm at the midpoint between the subcostal margin and the margin of the suprasternal plane according to the diagnostic criteria of the International Diabetes Federation (IDF). Height was measured to the nearest 0.1 cm using a portable stadiometer and weight was measured to the nearest 0.1 kg using calibrated platform scales. BMI was calculated as body weight (kg) divided by the square of height (m²).

Blood pressure measurements

Blood pressure (BP) was measured in the sitting position using a mercury sphygmomanometer with an appropriate cuff size. After a 5-min rest period, BP was measured three times, and the average of the three measurements was used for statistical analyses.

Questionnaire

All participants were administered a standardized questionnaire that provided information relating to occupation, medical history, past and current medication

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Waist circumference and incidence of hypertension in Chinese adults. Observations from the Kailuan Study

Abstract

Background. The Kailuan Study examined cardiovascular risk factors in a Chinese cohort comprising employees of the Kailuan Coal Group who underwent regular health examinations.

Patients and methods. Normotensive participants in the Kailuan study were enrolled in the present work and followed up for a median of 5.8 years to assess the development of hypertension (systolic blood pressure [SBP] ≥ 140 mmHg, diastolic blood pressure [DBP] ≥ 90 mmHg, or initiation of blood pressure [BP] medications).

Results. This study comprised a total of 50,024 participants (age, 47.9 ± 12.0 years;

male/female, 37,429/12,595), of whom 22,176 (44.3%) developed hypertension. In both male and female subjects, there was an increase in multivariable-adjusted hazard ratios for hypertension in all waist circumference (WC) groups (group 1, <70 cm; group 2, 70–79 cm; group 3, 80–89 cm; group 4, 90–99 cm; group 5, ≥ 100 cm). Results of a stratified analysis of subjects with normal body mass index (BMI; <24 kg/m²) showed that hazard ratios for hypertension still increased across WC groups. Significant interactions were found between WC groups and gender ($p < 0.001$), as well as between WC groups and BP categories ($p < 0.001$). Increased WC was

associated with a significantly higher risk of hypertension incidence in men compared with women and in subjects with a high-normal BP vs. those with an ideal BP.

Conclusion. WC is an independent predictor of hypertension incidence. The association between WC and hypertension incidence is affected by gender and baseline BP levels.

Keywords

Waist circumference · Hypertension · Body mass index · Gender · Obesity

Taillenumfang und Inzidenz der Hypertonie bei chinesischen Erwachsenen. Beobachtungen aus der Kailuan-Studie

Zusammenfassung

Hintergrund. In der Kailuan-Studie wurden die kardiovaskulären Risikofaktoren in einer chinesischen Kohorte untersucht, die aus Mitarbeitern der Kailuan Coal Group bestand und regelmäßig auf ihren Gesundheitszustand hin untersucht wurde.

Patienten und Methoden. Normotensive Teilnehmer der Kailuan-Studie wurden in die vorliegende Studie aufgenommen und im Mittel 5,8 Jahre lang nachbeobachtet, um zu ermitteln, ob sich eine Hypertonie entwickelte (systolischer Blutdruck ≥ 140 mmHg, diastolischer Blutdruck ≥ 90 mmHg oder Beginn der Gabe von Blutdruckmedikamenten).

Ergebnisse. Insgesamt wurden 50.024 Teilnehmer in diese Studie aufgenommen (Alter: $47,9 \pm 12,0$ Jahre; m./w.: 37.429/12.595), davon entwickelten 22.176 (44,3%) eine

Hypertonie. Sowohl bei männlichen als auch bei weiblichen Probanden gab es einen Anstieg der multivariabel angepassten Hazard-Ratio für Hypertonie in allen nach Taillenumfang unterteilten Gruppen (Gruppe 1: <70 cm; Gruppe 2: 70–79 cm; Gruppe 3: 80–89 cm; Gruppe 4: 90–99 cm; Gruppe 5: ≥ 100 cm). Ergebnisse einer stratifizierten Auswertung von Probanden mit normalem Body-Mass-Index (BMI; <24 kg/m²) zeigten, dass die Hazard-Ratio für Hypertonie quer durch die nach Taillenumfang unterteilten Gruppen weiterhin anstieg. Signifikante Wechselwirkungen fanden sich zwischen nach Taillenumfang unterteilten Gruppen und Geschlecht ($p < 0,001$) sowie zwischen nach Taillenumfang unterteilten Gruppen und Blutdruckkategorie ($p < 0,001$). Ein erhöhter

Taillenumfang ging mit einem signifikant erhöhten Inzidenzrisiko für Hypertonie bei Männern im Vergleich zu Frauen sowie bei Probanden mit einem hochnormalen Blutdruck gegenüber Probanden mit idealen Blutdruckwerten einher.

Schlussfolgerung. Der Taillenumfang ist ein unabhängiger Prädiktor für die Inzidenz der Hypertonie. Der Zusammenhang zwischen Taillenumfang und Inzidenz der Hypertonie wird durch Geschlecht und Ausgangsblutdruckwerte beeinflusst.

Schlüsselwörter

Taillenumfang · Hypertonie · Body-Mass-Index · Geschlecht · Adipositas

use, and personal habits such as cigarette and alcohol consumption.

Laboratory tests

Fasting venous blood samples were collected to measure glucose, uric acid, creatinine, and lipid levels (including total cholesterol, high-density lipoprotein cholesterol [HDL-C], and triglycerides).

Hypertension definition

Hypertension was defined as SBP ≥ 140 mmHg, DBP ≥ 90 mmHg, or the participant taking any antihypertensive medications. Antihypertensive medications were defined as any diuretic, alpha blocker, beta blocker, calcium channel blocker, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, nitrate, and hydralazine.

Data analysis

Statistical analyses were performed using R, version 3.1.1. Data are presented as mean (standard deviation [SD]) for continuous variables or proportions for categorical variables. We conducted Cox proportional-hazards analyses to estimate the hazard ratios and 95% confidence intervals for the development of hypertension in male and female subjects. WC was evaluated as a categorical variable

Table 3 Stratified analysis of multivariate hazard ratios for hypertension according to waist circumference in male and female subjects^a

		Waist circumference groups ^b					<i>p</i> for trend	<i>p</i> for interaction
		Group 1	Group 2	Group 3	Group 4	Group 5		
Male	<i>High blood pressure^c</i>							
	Yes	1	1.08 (0.92–1.28)	1.19 (1.01–1.40)	1.24 (1.05–1.47)	1.25 (1.04–1.49)	<0.001	<0.001
	No	1	1.14 (0.94–1.38)	1.42 (1.17–1.71)	1.64 (1.35–2.01)	1.54 (1.24–1.92)	<0.001	–
	<i>BMI ≥ 24 kg/m²</i>							
	Yes	1	0.94 (0.63–1.41)	1.15 (0.77–1.70)	1.32 (0.89–1.95)	1.44 (0.97–2.14)	<0.001	0.851
	No	1	1.16 (1.02–1.33)	1.33 (1.17–1.52)	1.41 (1.21–1.63)	1.37 (1.14–1.65)	<0.001	–
Female	<i>High blood pressure^c</i>							
	Yes	1	1.57 (1.21–2.05)	1.75 (1.34–2.28)	1.88 (1.42–2.48)	1.88 (1.40–2.54)	<0.001	<0.001
	No	1	1.26 (0.99–1.59)	1.54 (1.21–1.96)	1.68 (1.28–2.22)	1.33 (0.94–1.88)	0.003	–
	<i>BMI ≥ 24 kg/m²</i>							
	Yes	1	1.14 (0.68–1.92)	1.44 (0.87–2.41)	1.69 (1.01–2.83)	1.82 (1.08–3.08)	<0.001	0.884
	No	1	1.48 (1.22–1.78)	1.68 (1.38–2.05)	1.56 (1.19–2.04)	1.54 (1.14–2.09)	<0.001	–

^aThe multivariate Cox regression model was adjusted, if not stratified, for age, body mass index, systolic blood pressure, diastolic blood pressure, resting heart rate, glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, uric acid, creatinine, smoking, and alcohol consumption

^bWaist circumference groups: group 1, <70 cm; group 2, 70–79 cm; group 3, 80–89 cm; group 4, 90–99 cm; group 5, ≥100 cm

^cHigh blood pressure, systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥80 mmHg. *BMI* body mass index

Interaction terms between waist circumference groups and other factors were also evaluated, but none was found to be significant

(WC groups: group 1, <70 cm; group 2, 70–79 cm; group 3, 80–89 cm; group 4, 90–99 cm; group 5, ≥100 cm; or <80 cm, 80–89 cm, ≥90 cm in the Figure). Trend tests were computed by modeling the WC group medians as continuous variables. Interactions between covariables (as categorical variables) and WC were also evaluated. BMI categories were divided by 24 kg/m² using the criteria established by the Working Group on Obesity in China [19]; BP groups were defined as high-normal BP (SBP ≥130 mmHg or DBP ≥80 mmHg) and ideal BP (SBP <130 mmHg and DBP <80 mmHg). Interaction terms were computed by modeling the medians of the WC groups as continuous variables.

Results

The present study included 50,024 subjects (age: 47.9 ± 12.0 years, male/female 37,429/12,595). As shown in [Table 1](#), after a median follow-up of 5.8 years, 22,176 participants (44.3%) developed

hypertension, including 18,301 (48.9%) men and 3875 (30.8%) women. The mean value of WC was 85.0 cm (in all subjects): 86.4 cm in male and 80.8 cm in female subjects. All the covariates in the study included BMI, age, SBP, DBP, resting heart rate, glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol (LDL-C), HDL-C, uric acid, creatinine, smoking, and alcohol consumption.

As shown in [Table 2](#), in male subjects, age-adjusted hazard ratios for hypertension increased across the WC groups (group 1, <70 cm; group 2, 70–79 cm; group 3, 80–89 cm; group 4, 90–99 cm; group 5, ≥100 cm), reaching 2.60 (95% confidence interval, 2.28 to 2.96) for the top group as compared with the bottom group (*p* for trend <0.001). Further adjustments for BMI and BP (including SBP and DBP) attenuated the risk values. In a multivariate model further adjusted for resting heart rate, glucose, total cholesterol, triglycerides, LDL-C, HDL-C, uric acid, creati-

nine, smoking, and alcohol consumption (besides age, BMI, and BP) only mildly attenuated the risk values as compared with the previous model (adjusted for age, BMI, and BP). Similarly, in female subjects, age-adjusted hazard ratios for hypertension also increased across WC groups, reaching 3.46 (95% confidence interval, 2.83–4.23) for the top group as compared with the bottom group (*p* for trend <0.001). Further adjustments for BMI and BP also attenuated the risk values, which were only mildly attenuated in the multivariate model. The interaction term between WC groups and sex was significant (*p* for interaction <0.001): As shown in [Fig. 1a](#), women in the bottom group (WC <80 cm) showed the lowest risk while men in the top group (WC ≥90 cm) showed the highest risk. As WC increased, men compared with women had significantly higher risk of hypertension incidence.

The results of a stratified analysis of multivariate hazard ratios for hypertension according to WC groups are

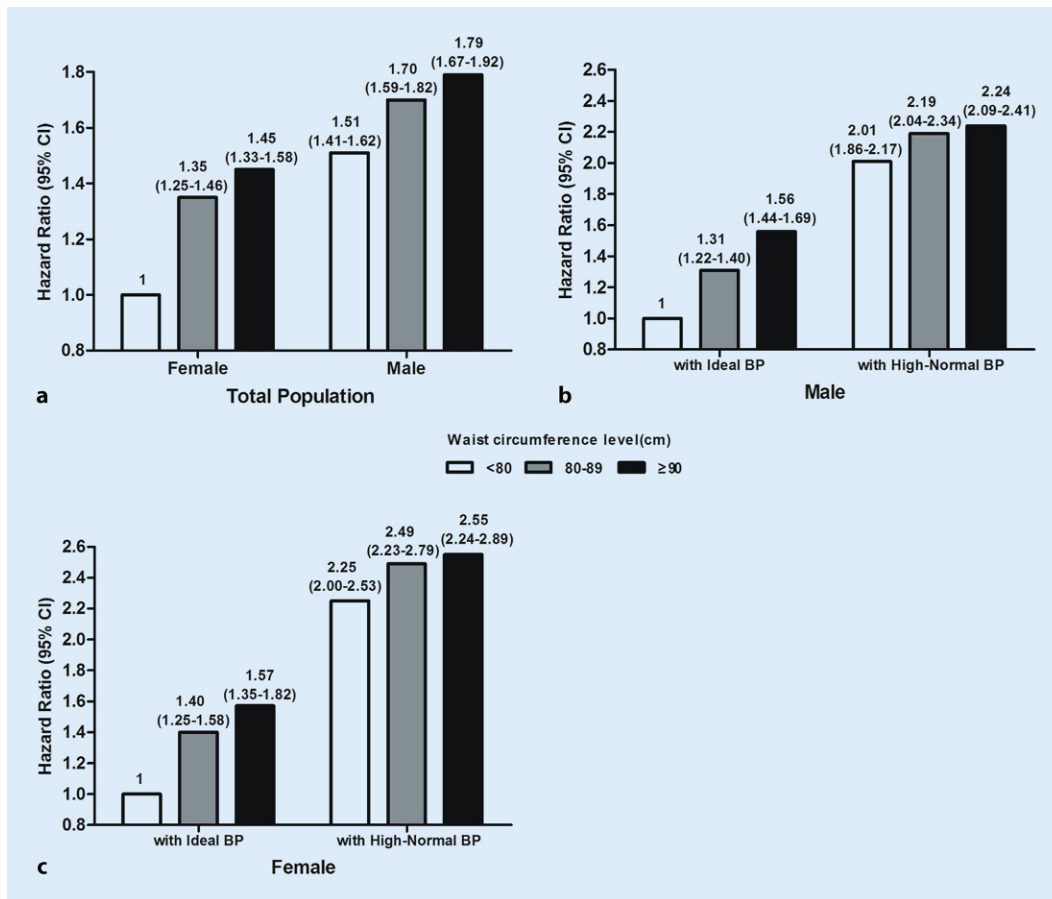


Fig. 1 ◀ Joint effect of waist circumference values, gender, and blood pressure levels in predicting hypertension. **a** Hazard ratios for hypertension according to waist circumference levels and gender. **b** Hazard ratios according to blood pressure (BP) levels; ideal BP: systolic blood pressure (SBP) <130 mmHg and diastolic blood pressure (DBP) <80 mmHg; high-normal BP: SBP ≥130 mmHg or DBP ≥80 mmHg in male subjects. **c** Hazard ratios according to BP levels in female subjects. The multivariate Cox regression model was adjusted, if not stratified, for age, body mass index, systolic blood pressure, DBP, resting heart rate, glucose, total cholesterol, triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, uric acid, creatinine, smoking, and alcohol consumption

shown in **Table 3**. In male subjects with high-normal BP (SBP ≥130 mmHg or DBP ≥80 mmHg) or ideal BP (SBP <130 mmHg and DBP <80 mmHg) at baseline, hazard ratios for hypertension increased across WC groups (p for trend <0.001). However, compared with men with ideal BP, those with high-normal BP had significantly higher risk of hypertension incidence: As shown in **Fig. 1b**, men with ideal BP in the bottom group (WC <80 cm) showed the lowest risk while men with high-normal BP in the top group (WC ≥90 cm) showed the highest risk. Similarly, as shown in **Fig. 1c**, women with high-normal BP also had significantly higher risk of hypertension incidence than those with ideal BP.

In all subjects (both male and female) with normal BMI (BMI <24 kg/m²), hazard ratios for hypertension increased across WC groups (group 1, <70 cm; group 2, 70–79 cm; group 3, 80–89 cm; group 4, 90–99 cm; group 5, ≥100 cm). Compared with group 1 (WC <70 cm),

group 2 (70 cm ≤ WC < 80 cm) already showed significantly higher risk of hypertension incidence, suggesting a much more tight control of WC is needed for decreasing hypertension risk. Interaction terms between WC groups with BMI or other factors were also evaluated in both male and female subjects, but none was found to be significant.

Discussion

This prospective study contributes several important findings. First, it shows that WC appears to be an important obesity-related predictor of hypertension incidence, and it increases the risk of hypertension in a dose-response fashion rather than only at high WC thresholds. Second, the association between WC and hypertension incidence is also affected by gender and baseline BP levels; as WC increased, men compared with women, and subjects (both male and female) with high-normal BP (SBP ≥130 mmHg or DBP ≥80 mmHg) compared with those

with ideal BP (SBP <130 mmHg and DBP <80 mmHg), showed significantly higher risk of hypertension incidence. Third, stratified analysis also showed that, in subjects (both male and female) with normal BMI (BMI <24 kg/m²) and low WC (WC <80 cm), the risk of hypertension still increased as WC increased.

Consistent with previous studies [20–23], the present research showed that WC, independent of BMI, was an important predictor of hypertension incidence in a Chinese population. For predicting obesity-related diseases (such as hypertension, stroke, heart disease, diabetes mellitus, and lipoprotein disorders), previous studies recommended Chinese-specific WC values ranging from 80.5 to 95.1 cm for men and 71.5 to 83.7 cm for women. However, in the present study, we found that, as WC increases, the risk of hypertension increases in a dose-response fashion, and both men and women in WC group 2 (70 cm ≤ WC <80 cm) had a higher risk than those in WC group 1 (WC

<70 cm), which suggested a lower WC cut-off point. Moreover, even in subjects with normal BMI (BMI <24 kg/m²), hazard ratios for hypertension still increased across WC groups (group 1, <70 cm; group 2, 70–79 cm; group 3, 80–89 cm; group 4, 90–99 cm; group 5, ≥100 cm).

Interestingly, all previous studies in Chinese populations [22–29] suggested lower WC values in women than in men, that is, a much more rigorous control of WC is needed in women than in men. However, in the present study, joint effects of gender and WC on hypertension risk showed that men had significantly higher risk of hypertension incidence as WC increased compared with women. Additionally, the association between WC and hypertension incidence is also affected by baseline BP levels, and subjects with high-normal BP compared with those with ideal BP showed a significantly higher risk of hypertension incidence, which suggests a much more rigorous control of WC in subjects with high-normal BP than those with ideal BP.

Although the biological mechanisms responsible for the association between WC and hypertension are still unknown, metabolic products of intra-abdominal adipose tissue, such as inflammatory adipokines, angiotensinogen (AGN), or cortisol, have been proposed [30]. Visceral adipose tissue produces a large amount of proinflammatory cytokines, AGN [31], leptin, reactive oxygen species [32], etc., and by doing so promotes activation of the sympathetic nervous system [33] and the renin-angiotensin system [34], insulin resistance, and metabolic syndrome [32], which are further linked to hypertension incidence.

Our study was limited in the following aspects. First, the Kailuan Study participants were predominantly from the Kailuan community in Tangshan, a city in the north of China, and thus the generalizability of our findings to other populations requires caution. Second, the present study mainly focused on the relationship between WC and hypertension incidence; future studies should further analyze the associations between WC and other obesity-related diseases.

Conclusion

In summary, our findings suggest that WC is an independent predictor of hypertension incidence, and it increases the risk of hypertension in a dose-response fashion rather than only at high WC thresholds. The association between WC and hypertension incidence is also affected by gender and baseline BP levels. Males and subjects with high-normal BP (SBP ≥130 mmHg or DBP ≥80 mmHg) should have a much more rigorous control of WC.

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Compliance with ethical guidelines

Conflict of interest. H. Sun, M. Zheng, S. Wu, M. Chen, J. Cai, and X. Yang declare that they have no competing interests.

The study was performed according to the guidelines of Helsinki Declaration and was approved jointly by the Ethics Committee of the Kailuan General Hospital and Beijing Chaoyang Hospital. Written informed consent was obtained from all participants.

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Hier steht eine Anzeige.