BMJ Open Association between neck circumference and cardiometabolic disease in Chinese adults: a community-based crosssectional study

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ABSTRACT Objectives

Objectives Several studies have indicated that neck circumference (NC) was associated with cardiometabolic disease in some Western countries. However, there are limited data regarding this association among Chinese adults.

Design A community-based cross-sectional study. **Setting** A multistage-stratified random cluster survey was conducted in Xixiang Street, Bao'an District of Shenzhen in southeast China.

Participants This study included 4000 participants (1605 men and 2395 women) with a mean age of 56.0±9.8 years.

Main outcome measures Categorical data were reported as percentage and continuous data were reported as mean±SD. Receiver operating characteristic analysis and logistic regression analysis were used to evaluate the association of NC with cardiometabolic disease. Results The mean NC values were 35.50±4.23 cm for men and 32.32±3.59 cm for women. After adjusting for body mass index and waist circumference, NC was significantly associated with the risk of hypertension (OR: 1.42 in women), decreased high-density lipoprotein (HDL) levels (OR: 1.27 in men; OR: 1.12 in women), high triglyceride (TG) levels (OR: 1.54 in women) and diabetes (OR: 1.41 in men; OR: 1.37 in women). Among men, the optimal NC cut-off values were 38.10 cm for identifying hypertension, 32.32 cm for decreased HDL levels, 36.6 cm for high TG levels and 36.6 cm for diabetes. Among women, the optimal NC cut-off values were 32.35 cm for identifying hypertension, 33.40 cm for decreased HDL levels, 32.90 cm for high TG levels and 33.40 cm for diabetes.

Conclusions NC was significantly associated with cardiometabolic disease in Chinese population. Although further studies are needed to confirm the optimal cut-off values, evaluating NC may be useful for predicting cardiometabolic disease risk during clinical assessments.

INTRODUCTION

Cardiometabolic disease such as diabetes, dyslipidaemia and cardiovascular disease^{1 2} are the common condition seen in primary care, which have increased substantially in recent years, and imposed heavy burden on

Strengths and limitations of this study

- This is the first study to explore optimal neck circumference cut-off values for discriminating diabetes and dyslipidaemia in this population.
- The present study is limited by its cross-sectional design, which precludes interpretation of the causality of the associations that were observed. Another limitation is that the participants were middle-aged and older Chinese adults, although similar results have been observed among younger subjects.
- Due to developing and validating using the same dataset, further population-based studies are needed to validate the diagnostic utility.

healthcare systems. Cardiometabolic disease is estimated to be responsible for a substantial proportion of morbidity and premature mortality globally.³⁻⁶ The causes of cardiometabolic disease are complex and correlated with numerous factors, with obesity being an established risk factor.⁷⁻¹⁰ Total body obesity and visceral obesity can be evaluated based on body mass index (BMI), waist circumference (WC) and waist-to-hip, which may predict the risk of cardiometabolic disease.^{11–14} However, recent studies have suggested upper-body subcutaneous adipose tissue, as estimated by neck circumference (NC) is more pathogenic than total body obesity and abdominal visceral fat.¹⁰¹⁵

NC measured at the inferior margin of the laryngeal prominence was a better indicator of obesity than the other anthropometric indexes,¹⁶ as it is a clear and convenient measurement at an explicit anatomical landmark that exhibits minimal fluctuations that are related to diet or respiratory conditions. Therefore, NC is a convenient tool for use in clinical settings, especially in primary health-care institutions.

To cite: Fu W, Zou L, Yin X, et al. Association between neck circumference and cardiometabolic disease in Chinese adults: a community-based crosssectional study. *BMJ Open* 2019;9:e026253. doi:10.1136/ bmjopen-2018-026253

Prepublication history and additional material for this paper are available online. To view these files, please visit the journal online (http://dx.doi. org/10.1136/bmjopen-2018-026253).

Received 25 August 2018 Revised 25 September 2019 Accepted 16 October 2019

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Recent studies have also indicated that NC was associated with hypertension, diabetes, metabolic syndrome and dyslipidaemia, which includes high total cholesterol (TC) levels, high triglyceride (TG) levels, high lowdensity lipoprotein cholesterol (LDL-C) levels and low high-density lipoprotein cholesterol (HDL-C) levels.^{15 17} However, there are limited data regarding these associations among Chinese adults, and the existing studies have mainly focused on the relationship between NC and hypertension.¹⁷⁻²⁰ Furthermore, some studies have used receiver operating characteristic (ROC) analysis to evaluate the accuracy of NC as diagnostic tests for cardiometabolic disease, and indicated that NC may be a valuable anthropometric index to predict cardiometabolic disease risk,^{16 21 22} although similar researches in China are scarce and no studies have identified the optimal cut-off values for predicting diabetes and dyslipidaemia in the Chinese population. Moreover, there are significant differences in the genetic backgrounds and criteria for obesity in the Asian and Western populations. China is the most populous nation in the world (with one-fifth of the world's population), similar researches in China are scarce and no studies have identified the optimal cut-off values for predicting diabetes and dyslipidaemia in the Chinese population. Therefore, the present study aimed to evaluate the relationship between NC and cardiometabolic disease among Chinese adults, and to establish NC cut-off values for predicting specific cardiometabolic diseases in the Chinese population.

METHODS

Patient and public involvement

This cross-sectional survey was conducted in the Bao'an District of Shenzhen (southeast China) between January 2015 and March 2016. Xixiang Street had 33 communities. TaoyuanJu, Liutang, Xixiang were selected in our study which should meet the following eligibility criteria: (1) the medical staff working in the community health service centre was proactive in engagement with the health education programme; (2) a well-maintained health record was provided and (3) it was located in either the national exemplary area of comprehensive prevention and control of chronic diseases or the national monitoring spot of chronic diseases. Subsequently, a multistage-stratified cluster survey was conducted on a random basis for each community. During the first-stage sampling, a computer program was applied to choose totally 4202 households at random among the three selected communities with the following requirements: (1) participants were required of a permanent residence for a minimum of 6 months annually in the community to ensure they could be contact and the age was restricted to 40 and over and (2) participants with mental disorder were prohibited from participation and the consent to survey participation was expressed. At the second-stage sampling, a random selection of suitable participants was conducted among each household that had been contacted for engagement with the interview.

Finally, all eligible participants were registered at the local government and informed to do laboratory examinations in community health centres at a specific time.

Data collection

A total of 4238 participants (1730 men and 2508 women) were recruited to undergo NC measurements, blood testing and a physical examination. In addition, participants completed a questionnaire regarding their age, sex, socioeconomic status, smoking, alcohol consumption habits and disease history. The physical examination included measurements of height, weight, NC and WC. Blood samples were obtained after an overnight fast to examine the participants' biochemical characteristics. Individuals were excluded if they had diagnosed illnesses, such as thyroid diseases, neck masses and deformities or malignant diseases. In addition, we excluded participants with implausible values for BMI ($<15 \text{ kg/m}^2$ and $>50 \text{ kg/m}^2$) and blood pressure (systolic blood pressure (SBP):<80 or >250 mm Hg, diastolic blood pressure (DBP):<40 or>150 mm Hg). Based on these exclusions, 4000 participants were included in the analyses.

Anthropometric and biomarker measurements

Each participant's horizontal NC was measured with their head erect and eyes facing forward, at the upper margin of the laryngeal prominence. Height without shoes was measured to the nearest 0.1 cm using a portable stadiometer. Weight in light clothing was measured to the nearest 0.1 kg using a digital scale. Each participant's WC was measured to the nearest 0.1 cm at the midpoint between the iliac crest and the lower rib.

All participants provided blood samples after a>8 hour overnight fast, which were collected into glass tubes and allowed to clot at room temperature. An enzymatic calorimetric test was used to measure the levels of TC, TG, LDL-C, HDL-C, fasting plasma glucose (FPG) and 2-hour post-load plasma glucose (2hPG) at a local hospital.

Blood pressure measurements and assessment of cardiometabolic disease

Blood pressure was measured after the participants had rested in a chair with back support for 10 min. Both feet were placed flat on the floor and the arms were supported at heart level while a trained nurse measured the blood pressure using an automated sphygmomanometer. Three measurements were taken at 5 min intervals during 08:00–09:00, and the mean value was recorded for the analyses. Participants were instructed to refrain from drinking alcohol, tea or coffee, smoking, or exercising for \geq 30 min before the evaluation.

Hypertension was defined as SBP $\geq 140 \text{ mm Hg}$, DBP $\geq 90 \text{ mm Hg}$ or the current use of antihypertensive medication.²³ Diabetes was defined as an FPG value $\geq 7.0 \text{ mmol/L}$, a 2hPG value $\geq 11.1 \text{ mmol/L}$ or current treatment using insulin or other hypoglycaemic agents.⁵ High TC was defined as a TC $\geq 6.22 \text{ mmol/L}$, high TG was defined as a measurement of 2.26 mmol/L or higher,

Table 1 Characteristics of the study participants stratified by gender					
Variable	Men (n=1605)	Women (n=2395)			
Age (years)	56.02±10.15	55.95±9.53			
BMI	24.53±3.07	24.06±3.48			
WC	85.46±9.10	80.42±9.81			
NC	35.50±4.23	32.32±3.59			
SBP	128.03±17.31	124.90±19.13			
DBP	84.66±11.74	80.37±11.09			
FPG	5.97±10.02	5.60±1.44			
TG	1.85±1.49	1.62±1.25			
TC	4.81±0.96	4.97±1.37			
LDL-C	3.65±1.21	3.49±1.15			
HDL-C	0.89±0.75	0.91±0.48			
2hPG	8.22±3.56	8.31±3.23			
Education					
Primary school	327 (20.4)	1004 (42.0)			
Junior high school	502 (31.3)	704 (29.4)			
High school	437 (27.1)	473 (19.7)			
Junior College	333 (20.7)	212 (8.8)			
Master degree	6 (0.4)	2 (0.08)			
Smoking					
No	1030 (64.2)	2364 (98.7)			
Yes	575 (35.8)	31 (1.3)			
Drinking					
No	1107 (69.0)	2302 (96.1)			
Yes	498 (31.0)	93 (3.9)			
Hypertension	492 (30.7)	520 (21.7)			
Decreased HDL	286 (17.8)	502 (21.0)			
High TG	354 (22.0)	343 (14.3)			
Diabetes	167 (10.4)	220 (9.2)			

Characteristics of the study particle state that if

Categorical data were reported as percentages and continuous data were reported as means \pm SD.

BMI, body mass index; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; 2hPG, 2-hour post-load plasma glucose; LDL-C, low-density lipoprotein cholesterol; NC, neck circumference; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides; WC, waist circumference.

increased LDL-C was defined as LDL-C $\geq\!\!4.14$ mmol/L and decreased HDL-C was defined as HDL-C $<\!\!1.04$ mmol/L. 24

Statistical methods

Categorical data were reported as number and percentage, while continuous data were reported as mean±SD. Partial correlation analysis was used to examine the correlations between NC and the cardiometabolic disease indexes. Logistic regression models were used to evaluate the association between NC and dichotomous cardiometabolic diseases. Model 1 only included NC. Model 2 was adjusted for age, sex, smoking, drinking and education. Model 3 was adjusted for BMI and the covariates in model 2. Model 4 was adjusted for WC and the covariates in model 2. Model 5 was adjusted for BMI, WC and the covariates in model 2. The optimal cut-off values and predictive abilities of NC were evaluated using ROC analysis, and the results were confirmed using logistic regression models to compare the associations between the NC categories and the cardiometabolic disease. All data were entered into a database in a double-blind manner by two different researchers, who used EpiData software (V.3.0). All statistical analyses were performed using SPSS software (V.19.0). Two-tailed pvalues were considered statistically significant at <0.05.

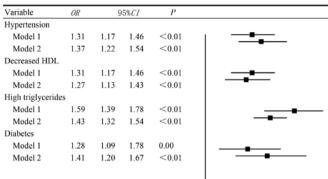
Results

Table 1 presents the participants' main characteristics. The mean age was 56.0±9.8 years (men: 56.02±10.15 years, women: 55.95±9.53 years). The overall average NC was 33.59 ± 4.16 cm, with average values of 35.50 ± 4.23 cm for men and 32.32±3.59 cm for women. Table 2 shows that there were several age-adjusted correlations between NC and the cardiometabolic disease indexes. Among men, NC was significantly correlated with SBP (r=0.112, p<0.01), DBP (r=0.185, p<0.01), FPG (r=0.115, p<0.01), 2hPG (r=0.132, p<0.01), TG (r=0.176, p<0.01), LDL-C (r=0.107, p<0.01), HDL-C (r=-0.087, p<0.01), smoking (r=0.066, p=0.011), drinking (r=0.067, p=0.007) and physical activity (r=0.101, p<0.01). However, NC was not significantly correlated with TC among men (r=0.01, p=0.709). The same significant correlations were observed among women, with the exception of the correlation between NC and LDL-C (r=0.034, p=0.11).

and the cardiometabolic disease indexes							
	Men		Women				
Variable	R	P value	R	P value			
SBP	0.112	<0.01	0.149	<0.01			
DBP	0.185	<0.01	0.133	<0.01			
FPG	0.115	<0.01	0.123	<0.01			
2hPG	0.132	<0.01	0.145	<0.01			
TG	0.176	<0.01	0.177	<0.01			
TC	0.010	0.709	0.022	0.292			
LDL-C	0.107	<0.01	0.034	0.110			
HDL-C	-0.087	<0.01	-0.054	0.010			
Smoking	0.066	0.011	0.054	0.010			
Drinking	0.067	0.077	0.056	0.008			
Physical activity	0.101	<0.01	0.067	0.001			

 Table 2
 Partial correlations between neck circumference

Pearson partial correlation coefficients, adjusted for age. DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-C, high-density lipoprotein cholesterol; 2hPG, 2-hour post-load plasma glucose; LDL-C, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; TG, triglycerides.



0.80 0.90 1.00 1.10 1.20 1.30 1.40 1.50 1.60 1.70 1.80

Figure 1 Neck circumference (continuous data) in relation to the risk of cardiometabolic disease in male patients. Model 1: unadjusted; model 2: adjusted for age, sex, smoking, drinking and education; NC, neck circumference (continuous data).

Multivariate logistic regression analysis was used to evaluate the associations between NC and cardiometabolic disease (figures 1 and 2). In the multivariate model (model 2), men with large NC values had elevated risks of hypertension (adjusted OR: 1.37, 95% CI 1.22 to 1.54), decreased HDL levels (OR: 1.27, 95% CI 1.13 to 1.43), high TG levels (OR: 1.43, 95% CI 1.32 to 1.54) and diabetes (OR: 1.41, 95% CI 120 to 1.67). Women with large NC values also had elevated risks of hypertension (OR: 1.42, 95% CI 1.28 to 1.58), decreased HDL levels (OR: 1.12, 95% CI 1.01 to 1.23), high TG levels (OR: 1.54, 95% CI 1.38 to 1.73) and diabetes (OR: 1.37, 95% CI 1.20 to 1.57).

The ROC analysis results are shown in table 3. Among men, the optimal NC cut-off values were 38.10 cm for hypertension (area under the curve (AUC): 0.567), 32.25 cm for decreased HDL levels (AUC: 0.573), 36.60 cm for high TG levels (AUC: 0.631) and 36.60 cm for diabetes (AUC: 0.557). Among women, the optimal NC cut-off values were 32.35 cm for hypertension (AUC: 0.606), 33.40 cm for decreased HDL levels (AUC: 0.537),

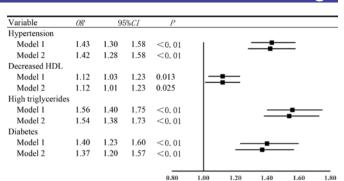


Figure 2 Neck circumference (continuous data) in relation to the risk of cardiometabolic disease in female patients. Model 1: unadjusted; model 2: adjusted for age, sex, smoking, drinking and education; NC, neck circumference (continuous data).

32.90 cm for high TG levels (AUC: 0.633) and 33.40 cm for diabetes (AUC: 0.596). Moreover, we evaluated the associations between the NC categories and the risks of cardiometabolic disease according to sex (table 4). After adjusting for age, sex, smoking, drinking, education, BMI and WC, both men and women with the high values for each NC category had elevated risks of the corresponding cardiometabolic disease index, with the exceptions of hypertension and high TG levels among men. Additionally, we analysed the risk of cardiometabolic disease per 1-SD increase in NC, WC and BMI in online supplementary table S1. We also compared the predictive value of NC, BMI and WC for hypertension, decreased HDL, high TG and diabetes in online supplementary table S2.

DISCUSSION

The present study found that NC was associated with cardiometabolic disease, regardless of adjustment for other confounders. Our study also indicated that BMI and WC are associated with cardiometabolic diseases.

Table 3Areas underdisease	er the rec	eiver operating c	haracteristic by	neck circumf	erence to iden	tify partic	ipants wit	h cardion	netabolic
Variable	AUC	95% CI	Cut-off point	Sensitivity	Specificity	PPV	NPV	+LR	–LR
Men									
Hypertension	0.567	0.536 to 0.598	38.10	0.242	0.856	0.426	0.408	1.681	0.886
Decreased HDL	0.573	0.543 to 0.603	32.25	0.889	0.238	0.324	0.839	1.167	0.466
High triglycerides	0.631	0.599 to 0.664	36.6	0.562	0.655	0.316	0.841	1.629	0.669
Diabetes	0.557	0.509 to 0.604	36.6	0.479	0.621	0.128	0.911	1.264	0.839
Women									
Hypertension	0.606	0.578 to 0.634	32.35	0.552	0.614	0.148	0.832	1.430	0.730
Decreased HDL	0.537	0.511 to 0.564	33.40	0.313	0.748	0.285	0.521	1.242	0.918
High triglycerides	0.633	0.602 to 0.664	32.90	0.586	0.614	0.201	0.899	1.518	0.674
Diabetes	0.596	0.556 to 0.636	33.40	0.4	0.747	0.138	0.925	1.580	0.803

AUC, area under the curve; +LR, positive likelihood ratio; -LR, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value; ROC, receiver operating characteristic.

	Men	Men			Women		
	OR	95% CI	P value	OR	95% CI	P value	
Hypertension							
Model 1	1.96	1.50 to 2.56	<0.01	1.99	1.63 to 2.44	<0.01	
Model 2	2.12	1.60 to 2.80	<0.01	1.98	1.61 to 2.41	<0.01	
Model 3	1.53	1.12 to 2.09	0.008	1.51	1.19 to 1.91	0.001	
Model 4	1.51	1.09 to 2.09	0.014	1.58	1.24 to 2.02	<0.01	
Model 5	1.41	1.01 to 1.95	0.043	1.51	1.19 to 1.96	0.001	
Decreased HDL							
Model 1	2.49	1.81 to 3.42	<0.01	1.35	1.10 to 1.66	0.004	
Model 2	2.31	1.66 to 3.20	<0.01	1.31	1.06 to 1.63	0.012	
Model 3	2.08	1.48 to 2.93	<0.01	1.20	0.95 to 1.52	0.130	
Model 4	2.19	1.55 to 3.08	<0.01	1.40	1.10 to 1.78	0.007	
Model 5	2.10	1.49 to 2.97	<0.01	1.31	1.03 to 1.68	0.030	
High triglycerides							
Model 1	2.47	1.94 to 3.14	<0.01	2.27	1.81 to 2.87	<0.01	
Model 2	2.34	1.82 to 3.00	<0.01	2.28	1.80 to 2.90	<0.01	
Model 3	1.61	1.20 to 2.17	0.001	1.95	1.50 to 2.55	<0.01	
Model 4	1.47	1.08 to 1.99	0.014	1.91	1.45 to 2.51	<0.01	
Model 5	1.36	1.00 to 1.87	0.050	1.96	1.49 to 2.55	<0.01	
Diabetes							
Model 1	1.51	1.09 to 2.08	<0.01	1.97	1.48 to 2.62	<0.01	
Model 2	1.87	1.33 to 2.63	<0.01	1.89	1.40 to 2.57	<0.01	
Model 3	1.75	1.19 to 2.59	0.004	1.8	1.29 to 2.52	0.001	
Model 4	1.58	1.05 to 2.37	0.027	1.66	1.17 to 2.36	0.005	
Model 5	1.59	1.05 to 2.41	0.027	1.67	1.17 to 2.38	0.005	

Model 1: unadjusted; model 2: adjusted for age, sex, smoking, drinking and education; model 3: adjusted for age, sex, smoking, drinking, education and BMI; model 4: adjusted for age, sex, smoking, drinking, education and WC; model 5: adjusted for age, sex, smoking, drinking, education, BMI and WC.

For hypertension, neck circumference <38.10 cm was the reference in men and neck circumference <32.35 cm was the reference in women. For decreased HDL, neck circumference <32.25 cm was the reference in men and neck circumference <33.4 cm was the reference in women. For high triglycerides, neck circumference <36.6 cm was the reference in men and neck circumference <32.9 cm was the reference in women. For diabetes, neck circumference <36.6 cm was the reference in men and neck circumference <33.4 cm was the reference in women. BMI, body mass index; HDL, high-density lipoprotein; WC, waist circumference.

Although BMI is widely used to define overweight and obesity, the criteria using BMI to determine obesity varies across different populations, which makes it unable to directly measure body fat or implicate the distribution of fat.^{25 26} WC is the most commonly used anthropometric parameter for evaluating abdominal adiposity, but either the structure of the abdominal wall or abdominal organs and cavity can be affected through the variations of WC in time and conditions. Moreover, it may not be applicable for study with large sample population, especially in cold weather people would wear heavy clothes.²⁷ Conversely, NC, as a simple, time-saving and stable anthropometric measurement, was a phenotype of upper body fat depot and it may also affect the cardiometabolic system.²⁸ Furthermore, the present study established several NC cut-off values for identifying cardiometabolic disease in

previous studies. For example, Preis *et al* found that, in the Framingham Heart Study of 2732 subjects, NC was related to hypertension, low HDL levels and diabetes.¹⁵ Selim *et al* also suggested that NC could be used to identify children with an elevated risk of cardiometabolic disease.²⁹ Furthermore, Cho *et al* evaluated 3521 middleaged Korean individuals and reported that NC was positively correlated with diabetes.³⁰ Lee and colleagues found that NC was associated with hypertension.³¹ He *et al* shown that NC is a tool for screening gestational diabetes mellitus.³² Those results, combined with our findings, shown that there were positive associations between NC and risks of hypertension, decreased HDL levels, high TG levels and diabetes.

this population. Similar results have been observed in

Several potential mechanisms have been proposed to explain the relationships between NC and cardiometabolic disease. For example, the lipolytic activity of upper body fat may explain the association of NC with hypertension.³³ In addition, obesity and elevated plasma levels of free fatty acids are associated with insulin resistance and increased very LDL production.^{13 34 35} Increased levels of free fatty acids are also correlated with markers of oxidative stress and vascular injury, and are associated with the development of hypertension.^{36 37} Furthermore, high NC values are a significant predictor of obstructive sleep apnea syndrome,³⁸ which has been associated with poor glycaemic control. This is because, even at the earliest stages of glucose intolerance, intermittent hypoxaemia and sleep fragmentation increase the risk of insulin resistance.

The present study revealed that NC was related to hypertension and high TG levels among men and women, although these relationships disappeared among men after adjusting for BMI and WC. This result does not agree with the findings from previous studies,¹⁸ ¹⁹ and this discrepancy may be related to differences in genetic background, dietary habits and the effects of other confounding factors. Moreover, these discrepancies could be related to the use of studies with cross-sectional designs, and prospective population-based studies are needed to address this issue.

In addition, the logistic regression models were used to evaluate the associations of the NC categories with the cardiometabolic disease indexes, which confirmed elevated risks of each index for individuals with NC values that exceeded the corresponding cut-off values. Therefore, it appears that NC is a tool for identifying cardiometabolic diseases, which provides evidences for future researches, but more studies are needed to verify the accuracy and effectiveness of NC as the predictor of cardiometabolic diseases. Moreover, to the best of our knowledge, this is the first study to establish the optimal NC cut-off values for predicting decreased HDL levels, high TG levels, and diabetes in a Chinese population, as previous studies have focused on detecting hypertension using NC. For example, Assyov *et al* reported that hypertension was predicted using NC cut-off values of ≥38 cm among Caucasian men and ≥ 35 cm among Caucasian women.³ A recent study of 2631 individuals in northeastern China also revealed that hypertension was predicted using NC cut-off values of >35.75 cm among men and >32.75 cm among women.¹⁹ Subsequent studies conducted in Korean population further confirmed the finding of Zhou et al that NC was a valuable index for identifying hypertension among Chinese adults.³² Thus, there appear to be population-specific variations in the optimal NC cut-off values, which were >38.10 cm among men and >32.25 cm among women in the present study. These discrepancies could be related to population-based differences in body size and composition.³⁶ Therefore, we suggest that future studies are needed to determine population-specific cutoff values for using NC to predict cardiometabolic disease.

CONCLUSION

The present study's results, combined with the findings of previous studies, indicate that NC is associated with cardiometabolic disease among Chinese adults. Thus, we recommend incorporating NC evaluations into clinical assessments. However, longitudinal studies are needed to validate the associations that we observed, and to establish population-specific cut-off values for using NC to predict cardiometabolic disease risk.

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Acknowledgements We thank all staff members and all participants involved in this study.

Contributors WF, YG and ZL conceived and designed the study. WF, XY, JM, SZ, LZ, SC, WL, YG and SY participated in the acquisition of data. WF analysed the data. XY and LZ gave advice on methodology. WF drafted the manuscript, and XY, YG and ZL revised the manuscript. All authors read and approved the final manuscript. ZL is the guarantor of this work and had full access to all the data in the study and take responsibility for its integrity and the accuracy of the data analysis.

Funding This study was supported by the Innovation Committee of Shenzhen Science and Technology, 'Demonstration Application of Cardiovascular and Cerebrovascular Disease Prevention and Control Based on Functional Community'(KJYY20170413162318686),and the FundamentalResearch Funds for the Central Universities, Huazhong University of Science and Technology, China. (2016YXMS215).

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Written informed consent was obtained from all individuals, and the study protocol was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No data are available.

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