RESEARCH

Large thigh circumference is associated with lower blood pressure in overweight and obese individuals: a community-based study

Jie Shi[1], Zhen Yang[1], Yixin Niu[1], Weiwei Zhang[1], Ning Lin[1], Xiaoyong Li[1], Hongmei Zhang[1], Hongxia Gu[1], Jie Wen[2], Guang Ning[3], Li Qin[1] and Qing Su[1]

[1]Department of Endocrinology, Xinhua Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China
[2]Department of Endocrinology and Metabolism, Institute of Endocrinology and Diabetes, Huashan Hospital, Fudan University, Shanghai, China
[3]Department of Endocrine and Metabolic Diseases, Shanghai Institute of Endocrinology and Metabolism, Shanghai Clinical Center for Endocrine and Metabolic Diseases, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China

Correspondence should be addressed to Z Yang or L Qin or Q Su: yangzhen@xinhuamed.com.cn or qinli@xinhuamed.com.cn or suqing@xinhuamed.com.cn

Abstract

Objective: A small thigh circumference is associated with an increased risk of diabetes, cardiovascular diseases, and total mortality. The purpose of this study was to evaluate the association between thigh circumference and hypertension in the middle-aged and elderly population.

Methods: A total of 9520 individuals aged 40 years and older with measurement of thigh circumference were available for analysis. The measurement of thigh circumference was performed directly below the gluteal fold of the thigh. The association of thigh circumference with hypertension was tested in logistic regression analyses and reported as odds ratio (OR) with 95% CI.

Results: Thigh circumference was negatively correlated with systolic blood pressure, diastolic blood pressure, fasting glucose, and total cholesterol. Compared with the lowest thigh circumference tertile group, the risk of hypertension was significantly lower in the highest tertile group, both in overweight individuals (OR 0.68; 95% CI 0.59–0.79, $P < 0.001$) and obese individuals (OR 0.51; 95% CI 0.38–0.70, $P < 0.001$).

Conclusion: In the present study, large thigh circumference is associated with lower risk of hypertension in overweight and obese Chinese individuals.

Key Words

► thigh circumference
► hypertension
► overweight
► obesity

Introduction

Hypertension, characterized by chronically elevated blood pressure (BP) above 140/90 mmHg, is a major public health problem affecting more than 1 billion people worldwide (1, 2). Despite multiple methods to prevent and manage high blood pressure, the global incidence and prevalence of hypertension continues to increase significantly (3). Convincing evidence demonstrated that hypertension, untreated or uncontrolled, is a crucial contributor to cardiovascular disease, stroke, and chronic kidney diseases (2). Consequently, hypertension is the leading cause of mortality and disability globally, which results in a huge health burden (4). Startlingly, more than half of individuals with elevated BP were unaware of their hypertensive status in numerous surveys, partly owing to hypertension rarely showing symptoms in the early stages (3, 4, 5). Hence, hypertension is a silent killer.

Previous research has demonstrated that intra-abdominal visceral deposition of adipose tissue, which characterizes upper-body obesity, plays a significant role in the development of hypertension (6, 7). Conversely, subjects with lower-body obesity exhibited a favorable metabolic profile (8). Due to the advantages of simplicity,

convenience, harmlessness, and low cost, anthropometric measurements, especially circumferences, are useful options for estimating fat distribution and body composition, particularly in large-scale population-based studies. Certain circumferences have shown good performance in evaluating nutritional status, assessing obesity, screening for ectopic lipid deposits, and identifying decline of muscle mass (9, 10, 11). Moreover, some abnormal circumferences are marks of increased risk of certain diseases (12). For instance, a small thigh circumference was associated with greater risk of diabetes (13), cardiovascular diseases, and total mortality (14) in both men and women. Additionally, it is well established that waist circumference is positively correlated with blood pressure (15) and that a high waist–thigh circumference ratio is a risk factor for hypertension (16). Data indicate that thigh circumference may be an indicator of hypertension.

To date, however, evidence from large-scale populations about the association between thigh circumference and hypertension is scarce. The aim of the present study was to examine the relationship between thigh circumference and blood pressure.

Methods

Study population

The study is a part of the Risk Evaluation of cAncers in Chinese diabeTic Individuals: A lONgitudinal (REACTION) study, which was a community-based cross-sectional study conducted among 259,657 Chinese individuals aged 40 years and older, from 2011 to 2012 (17). The study design and methods have been described previously in detail (17, 18, 19). The data presented in this study are based on the baseline survey of subsamples from the Chongming District in Shanghai, China. A total of 9930 eligible subjects participated in the research. The individuals with data missing for thigh circumference, blood pressure (BP), and metabolic variables were excluded. The final model included 9520 subjects (3095 men and 6425 women).

Data collection

A standardized questionnaire was used by certified medical workers to gather essential information, including sex, age, smoking and alcohol consumption habits, physical activity, education status, and previous medical history. Anthropometric measurements were performed by trained

physicians using standard protocols. Thigh circumference was measured directly below the gluteal fold of the thigh. The final thigh circumference is the average value of left thigh circumference and right thigh circumference. BP was measured with an automated electronic device (OMRON Model1 Plus; Omron Company, Kyoto, Japan) after the subjects sat down and rested quietly for >5 min. BP measurements were taken three times and the mean was recorded as the BP result. Overweight was defined as $24\ kg/m^2 \leq BMI < 28\ kg/m^2$ and obesity was defined as $BMI \geq 28\ kg/m^2$.

Biochemical measurements

Peripheral venous blood samples were collected after 10 h of overnight fasting. Plasma glucose level was assessed by the glucose oxidase method (ADVIA-1650 Chemistry System, Bayer). Triglycerides, low-density lipoprotein cholesterol (LDL-c), high-density lipoprotein cholesterol (HDL-c), and total cholesterol were measured by an automatic analyzer (Hitachi 7080). Fasting insulin was assessed by RIA (Linco Research). Insulin resistance was evaluated by the homeostasis model of assessment for insulin resistance (HOMA-IR).

Definition of hypertension

Hypertension was defined as a systolic blood pressure $(SBP) \geq 140$ mmHg, a diastolic blood pressure $(DBP) \geq 90$ mmHg, or current use of antihypertensive medications (20).

Statistical analysis

Normally distributed continuous variables were presented as means±S.D., and variables with skewed distribution were reported as medians (interquartile range) and log transformed to approximate normality before analysis. Categorical variables were described by percentage (%). *P* values were calculated by Student's *t*-test (for continuous parametric variables) or nonparametric Mann–Whitney *U* test (for continuous nonparametric variables) and by Chi-squared tests for categorical variables. Multiple linear regression analyses were used to assess the association between thigh circumference and metabolic features. Multivariate logistic regression models were applied to estimate the odds ratios (ORs) for hypertension. Potential confounding variables including age, gender, smoking, alcohol drinking, physical activity, educational status, C-reactive protein (CRP), adiponectin, BMI, and HOMA-IR were controlled in the regression models.

Data management and statistical analysis were performed with SPSS software (version 23.0). The significance level was set at $P<0.05$, and P values were provided for two-sided tests.

Ethics statement

The study protocol was approved by the Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine. Written informed consent was obtained from all participants.

Results

Characteristics of participants with or without incident hypertension

The mean thigh circumference was 53.3 ± 5.0 cm for men and 52.6 ± 4.7 cm for women ($P<0.001$), respectively. Subjects with hypertension were more likely to be older,

a smoker, and with a higher BMI, waist circumference, fasting blood glucose, HOMA-IR, total cholesterol and triglyceride level (Table 1).

The thigh circumference of hypertensive patients is lower than normotensive subjects

Compared with normotensive individuals, the thigh circumference of subjects with hypertension was lower (normal weight: 51.2 ± 4.2 cm vs 50.9 ± 4.2 cm, $P=0.011$; overweight: 53.9 ± 4.4 cm vs 53.3 ± 4.4 cm, $P<0.001$; obese: 56.6 ± 5.1 cm vs 55.4 ± 5.5 cm, $P<0.001$) (Fig. 1).

Large thigh circumference is associated with lower prevalence of hypertension in overweight and obese individuals

The subjects were divided into three groups (T1, T2, and T3) according to the tertiles of thigh circumference.

Table 1 Baseline characteristics of the study participants.

Characteristics	Men			Women		
	Normotension	Hypertension	*P* value	Normotension	Hypertension	*P* value
n	1363	1732		3586	2839	
Age, year(s)	56.23 ± 7.71	58.83 ± 7.24	<0.001	53.49 ± 7.68	57.90 ± 7.23	<0.001
Smoking (yes), %	39.5	45.7	0.005	3.8	5.9	<0.001
Alcohol (yes), %	48.3	48.9	0.392	10.2	10.6	0.08
Education, %						
0–6	16.1	21.3	0.001	19	30.1	<0.001
7–9	51.5	48.5		48.8	49.2	
≥10	32.4	30.2		32.3	20.7	
Physical activity						
Low	70.2	71.6	0.541	72.3	72.9	0.536
Moderate	21.7	20.1		20.2	19.9	
High	8.1	8.3		7.5	7.2	
SBP, mmHg	121 ± 10	144 ± 17	<0.001	118 ± 11	144 ± 16	<0.001
DBP, mmHg	77 ± 7	87 ± 9	<0.001	75 ± 7	85 ± 10	<0.001
BMI, kg/m^2	24.04 ± 3.20	25.62 ± 3.23	<0.001	23.80 ± 2.93	25.46 ± 3.28	<0.001
Waist circumference, cm	85.2 ± 9.5	89.8 ± 9.5	<0.001	80.9 ± 9.5	86.4 ± 11.4	<0.001
WHR	0.89 ± 0.07	0.91 ± 0.06	<0.001	0.85 ± 0.08	0.09 ± 0.16	<0.001
FPG, mmol/L	6.35 ± 1.79	6.73 ± 1.91	<0.001	5.91 ± 1.34	6.49 ± 1.82	<0.001
Insulin, µU/L	5.40 (3.80–7.70)	6.50 (4.50–9.00)	<0.001	6.40 (4.80–8.60)	7.70 (5.60–10.70)	<0.001
HOMA-IR	1.53 (0.99–2.30)	1.88 (1.29–2.75)	<0.001	1.65 (1.24–2.38)	2.24 (1.54–3.19)	<0.001
CRP, µg/mL	4.89 ± 6.12	5.24 ± 6.18	0.462	4.63 ± 5.39	5.27 ± 6.11	0.427
Adiponectin, µg/mL	12.6 (7.9–15.7)	10.9 (6.7–13.2)	0.023	11.9 (7.2–14.6)	9.5 (6.2–12.6)	0.014
Triglycerides, mmol/L	1.32 (0.94–2.04)	1.53 (1.06–2.33)	<0.001	1.19 (0.87–1.73)	1.52 (1.09–2.20)	<0.001
TC, mmol/L	4.49 ± 0.99	4.61 ± 1.01	0.002	4.58 ± 1.04	4.85 ± 1.03	<0.001
LDL-c, mmol/L	2.53 ± 0.73	2.58 ± 0.75	0.077	2.58 ± 0.77	2.72 ± 0.79	0.094
HDL-c, mmol/L	1.17 ± 0.32	1.15 ± 0.32	0.066	1.26 ± 0.31	1.24 ± 0.31	0.097
Thigh circumference, cm	53.2 ± 5.0	53.4 ± 5.1	0.143	52.6 ± 4.5	52.6 ± 4.7	0.825

Continuous data are shown as means ± S.D. or medians with interquartile range and categorical data as percentage (%). *P* values were calculated by Student's *t*-test (for continuous parametric variables) or nonparametric Mann–Whitney *U* test (for continuous nonparametric variables) and by Chi-squared tests for categorical variables.
CRP, C-reactive protein; DBP, diastolic blood pressure; FPG, fasting plasma glucose; HDL-c, high-density lipoprotein cholesterol; HOMA-IR, the homeostatic model assessment of insulin resistance; LDL-c, low-density lipoprotein cholesterol; SBP, systolic blood pressure; TC, total cholesterol; WHR, waist–hip ratio.
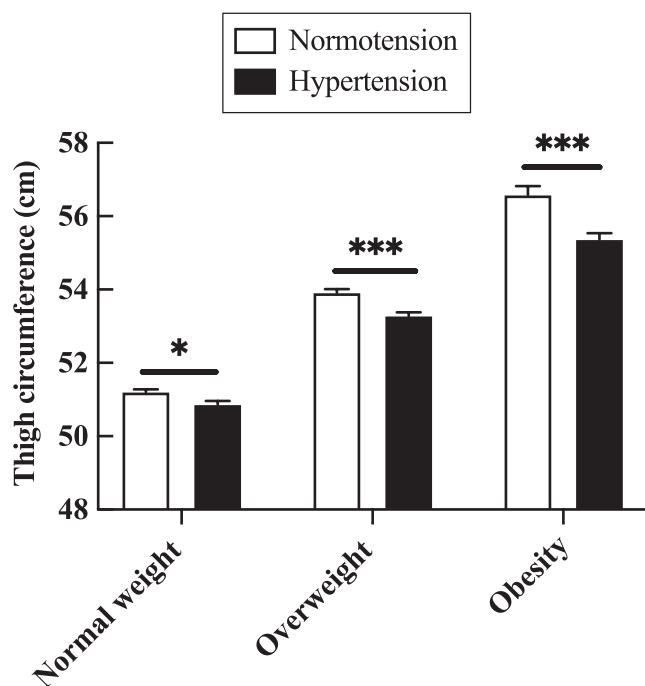
Figure 1
The thigh circumference was smaller in subjects with hypertension than individuals with normotension. Data are presented as mean ± S.E.M. *P* values were calculated by Student's *t*-test. *$P < 0.05$; **$P < 0.01$, ***$P < 0.001$.

The tertile ranges of thigh circumference were ≤51.2, 51.2–55.3, and ≥55.3 cm in men and ≤50.7, 50.7–54.4, and ≥54.4 cm in women, respectively. Along with the increased tertile of thigh circumference, the prevalence of hypertension gradually decreased in both overweight (men: 64.6% vs 61.3% vs 55.1%, $P=0.046$; women: 53.8% vs 48.1% vs 43.5%, $P=0.004$) and obese individuals (men: 79.5% vs 75.2% vs 71.5%, $P=0.047$; women: 74.5% vs 69.3% vs 59.0%, $P<0.001$).

We used multivariate logistic regression models, with the lowest tertile group (T1) as a reference, to evaluate the association between thigh circumference and risk of incident hypertension. As is shown in Table 2, the ORs for hypertension decreased when thigh circumference tertiles increased ($P<0.001$). In the highest tertile group (T3), the OR (95% CI) for hypertension was 0.83 (0.71–0.96) in overweight individuals and 0.56 (0.41–0.75) in obese individuals compared with the T1 group, after adjusting for age, gender, smoking, alcohol consumption, education status, physical activity, CRP, and adiponectin (Model 2). Moreover, after further adjustment for BMI and waist circumference, the association between thigh circumference and hypertension remained statistically significant in overweight individuals (OR 0.68; 95% CI, 0.59–0.79; $P<0.001$) and obese individuals

(OR 0.51; 95% CI, 0.38–0.70; $P<0.001$) (Model 4). Therefore, large thigh circumference was associated with a lower risk of hypertension among overweight and obese individuals, independent of BMI and waist circumference. Additionally, the correlation between thigh circumference and hypertension was stronger in obese individuals than in overweight individuals (Fig. 2). However, we did not observe a significant association between thigh circumference and hypertension in normal weight individuals ($P>0.05$).

Subgroup analyses

To evaluate the effect of waist circumference on the association of thigh circumference and blood pressure, we further combined thigh circumference and waist circumference in statistical analysis. We divided participants into four subgroups based on the medians of thigh circumference and waist circumference. The OR for hypertension was lower in the large thigh circumference with small waist circumference subgroup than in other subgroups (OR 0.52; 95% CI, 0.43–0.63; $P<0.001$) after adjustment for age, sex, life factor, CRP, adiponectin, and BMI in overweight and obese individuals (Fig. 3). Individuals with small thigh circumference and large waist circumference form the reference group.

Thigh circumference is negatively correlated with SBP and DBP

Multiple linear regression analyses indicated that thigh circumference was positively correlated with HDL-c, triglycerides, and insulin and was negatively correlated with SBP, DBP, fasting glucose, and total cholesterol (Table 3).

Discussion

In this study, we found that large thigh circumference is significantly associated with lower prevalence of hypertension in overweight and obese individuals, independent of age, BMI, and waist circumference. Moreover, thigh circumference is negatively correlated with both SBP and DBP.

Differences in body fat distribution patterns have long been linked to certain metabolic disease risks (21, 22). Previous studies have reported that upper-body and lower-body fat have opposite (harmful vs beneficial) correlations with long-term blood pressure

Table 2 Adjusted ORs (95% CI) of hypertension according to tertiles of thigh circumference.

Characteristics	T1 (n = 3177)	T2 (n = 3187)	T3 (n = 3156)	P value for trend
Normal weight (n = 4172)				
Model 1	1	0.97 (0.84–1.12)	1.05 (0.87–1.26)	0.72
Model 2	1	1.02 (0.87–1.20)	1.09 (0.98–1.35)	0.21
Model 3	1	0.91 (0.79–1.06)	0.95 (0.78–1.14)	0.49
Model 4	1	0.91 (0.78–1.06)	0.94 (0.78–1.13)	0.45
Overweight (n = 3864)				
Model 1	1	0.87 (0.76–0.99)	0.86 (0.75–0.98)	0.024
Model 2	1	0.86 (0.75–0.99)	0.83 (0.71–0.96)	0.020
Model 3	1	0.85 (0.73–0.99)	0.69 (0.59–0.81)	<0.001
Model 4	1	0.83 (0.72–0.95)	0.68 (0.59–0.79)	<0.001
Obese (n = 1484)				
Model 1	1	0.67 (0.48–0.93)	0.57 (0.42–0.77)	0.001
Model 2	1	0.65 (0.46–0.90)	0.56 (0.41–0.75)	0.001
Model 3	1	0.64 (0.46–0.89)	0.52 (0.38–0.70)	<0.001
Model 4	1	0.63 (0.45–0.88)	0.51 (0.38–0.70)	<0.001

Model 1: adjusted for age and sex; Model 2: further adjusted for smoking, drinking, physical activity, education status, CRP, and adiponectin; Model 3: further adjusted for BMI; Model 4: further adjusted for waist circumference. T1 is the reference group. Multivariate logistic regression models were applied.

and the risk of developing diabetes (23). Advanced and accurate measuring techniques such as dual-energy X-ray absorptiometry and CT are often used to assess body fat and muscle distribution. However, these sophisticated, time-consuming, and costly techniques are not always feasible, particularly in large-scale population studies. Due to convenience, harmlessness, and low cost, simple anthropometric measurements, such as waist circumferences, are often preferable. Large waist circumference is a proxy of abnormal accumulation of visceral fat along with adverse metabolism (15, 24).

Conversely, large thigh circumference is considered to be protective for diabetes and cardiovascular disease, and a small thigh circumference seems to be associated with an increased risk of developing heart disease (14, 25).

There are two likely causes for the hypertensive risk difference between different thigh circumference groups. On the one hand, a small thigh circumference may involve low subcutaneous thigh fat. Several studies reported that, independently of high abdominal fat,
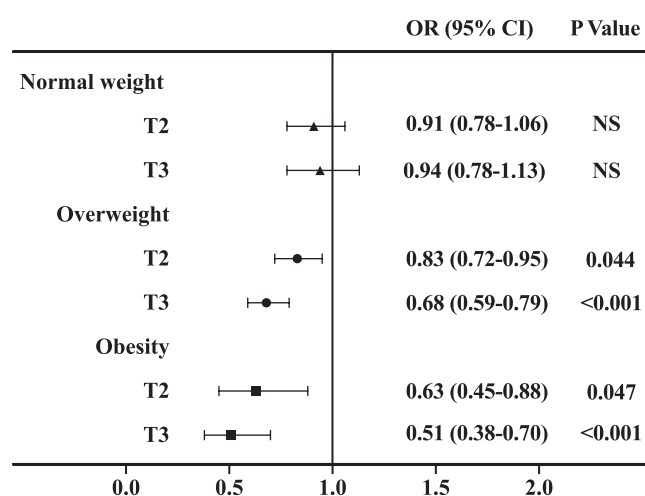
Figure 2
Adjusted ORs of hypertension according to tertiles of thigh circumference. The ORs with corresponding 95% CIs were adjusted for age, gender, life factors, CRP, adiponectin, BMI, and waist circumference. T1 is the reference group.
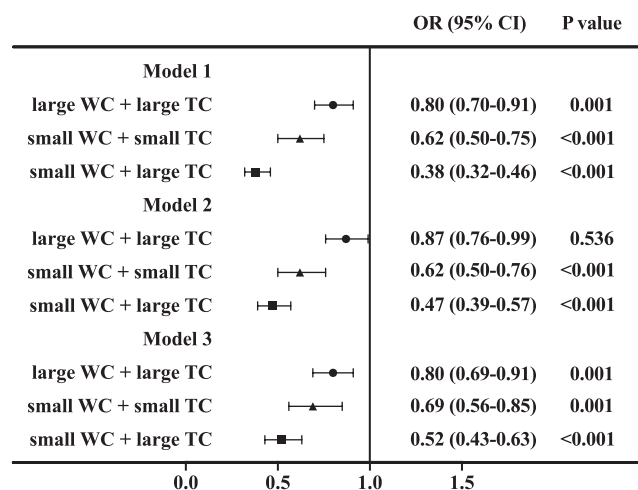
Figure 3
The association of thigh circumference with hypertension in different subgroups of waist circumference. WC, waist circumference; TC, thigh circumference. Model 1 was unadjusted; Model 2 was adjusted for age, sex, life factor, CRP, and adiponectin; Model 3 was further adjusted for BMI. Large waist circumference with small thigh circumference is the reference group.

Table 3 Adjusted regression coefficients of thigh circumference with metabolic parameters.

	Model 1		Model 2		Model 3		Model 4	
	β (s.e.m.)	P	β (s.e.m.)	P	β (s.e.m.)	P	β (s.e.m.)	P
SBP (mmHg)	−0.143 (0.084)	<0.001	−0.146 (0.089)	<0.001	−0.145 (0.090)	<0.001	−0.160 (0.089)	<0.001
DBP (mmHg)	−0.102 (0.046)	<0.001	−0.111 (0.049)	<0.001	−0.110 (0.049)	<0.001	−0.123 (0.049)	<0.001
FPG (mmol/L)	−0.032 (0.005)	0.020	−0.033 (0.005)	0.018	−0.034 (0.005)	0.013	−0.040 (0.005)	0.004
2-h glucose (mmol/L)	0.029 (0.020)	0.268	0.049 (0.021)	0.086	0.050 (0.021)	0.079	0.047 (0.021)	0.099
Insulin (μU/mL)	0.145 (0.016)	<0.001	0.153 (0.016)	<0.001	0.122 (0.017)	<0.001	0.098 (0.017)	<0.001
HOMA-IR	0.122 (0.006)	<0.001	0.136 (0.005)	<0.001	0.107 (0.006)	<0.001	0.084 (0.006)	<0.001
TC (mmol/L)	−0.115 (0.005)	<0.001	−0.116 (0.005)	<0.001	−0.119 (0.005)	<0.001	−0.119 (0.005)	<0.001
LDL-c (mmol/L)	−0.021 (0.004)	0.422	−0.018 (0.004)	0.529	−0.018 (0.004)	0.539	−0.018 (0.004)	0.536
HDL-c (mmol/L)	0.276 (0.001)	<0.001	0.281 (0.001)	<0.001	0.280 (0.001)	<0.001	0.282 (0.001)	<0.001
Triglycerides (mmol/L)	0.068 (0.003)	<0.001	0.070 (0.003)	0.013	0.068 (0.001)	0.016	0.063 (0.001)	0.025

Fasting insulin, HOMA-IR, and triglycerides were log-transformed before analysis. Model 1: adjusted for age, sex. Model 2: further adjusted for smoking, drinking, physical activity, education status, CRP, and adiponectin. Model 3: further adjusted for BMI. Model 4: further adjusted for waist circumference. Multiple linear regression analyses were used.

low subcutaneous thigh fat contributed to adverse lipid and glucose metabolism, while high subcutaneous thigh fat was associated with favourable lipid and glucose metabolism (26). It is established that thigh subcutaneous adipose is negatively associated with fasting glucose, post load glucose, and HOMA-IR (27, 28). Moreover, greater thigh-fat deposition exhibited a more favorable metabolic profile including lower triglycerides and LDL-c (26), and thigh adipocytes were resistant to epinephrine-stimulated lipolysis, presumably due to an increase in alpha-adrenergic receptors (29). Therefore, the adverse glucose and lipid metabolism that mediates vascular dysfunction may link low thigh circumference to increased risk of elevated blood pressure.

On the other hand, small thigh circumference may indicate a low thigh skeletal muscle mass, which is closely associated with increased risk factors for hypertension and diabetes (30, 31). Clear evidence demonstrated that obese individuals with sarcopenia have a higher risk of hypertension than patients with obesity or sarcopenia alone (31, 32). Obesity increases the risk of hypertension, a decline in thigh skeletal muscle mass increases this risk further. This may partially explain why we only found a stronger correlation of small thigh circumference and increased risk of developing hypertension in overweight and obese subjects. Additionally, skeletal muscle is the predominant site for insulin-stimulated glucose uptake, a lower thigh skeletal muscle mass may induce or promote dysfunctional glucose metabolism.

The major strength of this study is that the analysis is performed in different BMI classifications. Many potential covariates were considered in the analysis to minimize the impact of confusing risk factors. However, there are several

potential limitations to consider in this study. First, we could not quantify the thigh muscle mass, intermuscular adipose tissue, and subcutaneous fat accumulation by more accurate radiographic measures owing to limitations of epidemiological screening conditions. Therefore, the amount and size of thigh subcutaneous adipocyte and intermuscular adipocyte and thigh muscle mass are not clear. Second, since the current study is a cross-sectional analysis, we cannot draw conclusions on causality from our findings. Third, it is unclear whether our findings in overweight and obese middle-aged and older Chinese subjects can be generalized to normal-weight or younger people of other ethnicities.

Conclusions

In summary, large thigh circumference is independently associated with lower prevalence of hypertension, while small thigh circumference is linked to higher prevalence of hypertension in overweight and obese Chinese individuals. Based on the observations, it is necessary to include thigh circumference in routine anthropometric measurements, when evaluating populations at high risk of hypertension, cardiovascular diseases, or diabetes.

Availability of data

This study is a part of the Risk Evaluation of cAncers in Chinese diabeTic Individuals: A lONgitudinal (REACTION) study. All data analyzed in this study are based on REACTION study. The data are held in a secure and confidential database that can only be assessed by members of the REACTION group. The REACTION study website is http://www.rjh.com.cn/pages/neifenmike/REACTION/index.shtml.

Ethics approval and consent to participants

This study protocol was approved by the Ethics Committee of Xinhua Hospital Affiliated to Shanghai Jiaotong University School of Medicine. Written informed consent was obtained from all participants.

Author contribution statement

Z Y, L Q, and Q S designed the study. Y N, W Z, X L, H Z, N L, H G, J W, and G N recruited the subjects, processed samples, and contributed to acquisition of data. Z Y and J S analyzed the data. J S wrote the manuscript. Z Y revised the manuscript.

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