

Correlation between Waist Circumference and Carotid Intima-Media Thickness in Women from Shanghai, China*

SHEN Yun^{1,§}, ZHANG Lei^{1,§}, ZONG Wen Hong², WANG Zheng³, ZHANG Yin⁴,
YANG Man Jing⁵, MA Xiao Jing¹, ZHU Jia An⁶, BAO Yu Qian^{1,#}, and JIA Wei Ping¹

1. Department of Endocrinology and Metabolism, Affiliated Sixth People's Hospital of Shanghai Jiaotong University; Shanghai Clinical Center for Diabetes; Shanghai Diabetes Institute; Shanghai Key Laboratory of Diabetes Mellitus; Shanghai 200233, China; 2. Public Health Bureau of Shanghai Zhabei District, Shanghai 200070, China; 3. Gonghexin Road Community Health Service Center, of Shanghai Zhabei District, Shanghai 200072, China; 4. Tianmuxi Road Community Health Service Center of Shanghai Zhabei District, Shanghai 200070, China; 5. Daning Road Community Health Service Center of Shanghai Zhabei District, Shanghai 200072, China; 6. Department of Ultrasound, Affiliated Sixth People's Hospital of Shanghai Jiaotong University; Shanghai Institute of Ultrasonic Medicine, Shanghai 200233, China

Abstract

Objective To evaluate whether waist circumference (WC) ≥ 85 cm is related to asymptomatic preclinical atherosclerosis in women from Shanghai, China.

Methods A total of 2365 females aged ≥ 20 years recruited from 4 communities underwent physical examination and carotid artery scanning. Their carotid intima-media thickness (C-IMT) was measured.

Results The C-IMT was significantly higher in overweight or obese women with their BMI ≥ 25.0 kg/m² ($P < 0.01$) and in those with their WC ≥ 85 cm than in those with their WC < 85 cm ($P < 0.01$). Spearman and partial correlation analysis showed that the C-IMT was significantly correlated with WC which was independent of menopausal status. The C-IMT significantly increased with the increasing WC and reached to a platform in about 85 cm. An increment tendency was found in the subgroup with its WC < 85 cm ($P < 0.01$) while no significant tendency was found in the subgroup with its WC ≥ 85 cm ($P = 0.07$). Multiple stepwise regression analysis showed that the WC was an independent risk factor for C-IMT. In logistic regression model, the odd ratio of WC ≥ 80 cm, ≥ 80 cm and < 85 cm and ≥ 85 cm for evaluating the risk of C-IMT elevation was 1.632, 1.501, and 1.878, respectively.

Conclusion WC is significantly correlated with C-IMT in women from Shanghai, China, and WC ≥ 85 cm may be used in identifying the risk of subclinical carotid atherosclerosis.

Key words: Visceral obesity; Waist circumference; Carotid intima-media thickness

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#Correspondence should be addressed to BAO Yu Qian. Tel: 86-21-64369181. Fax: 86-21-64368031. E-mail: byq522@163.com

§SHEN Yun and ZHANG Lei contributed equally to this work.

Biographical notes of the first authors: SHEN Yun, male, born in 1987, M. D. candidate, majoring in obesity and metabolic syndrome; ZHANG Lei, male, born in 1978, M. D., majoring in endocrinology and metabolism.

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INTRODUCTION

Obesity is a worldwide public health concern. There is evidence that obesity can lead to metabolic and cardiovascular diseases, especially metabolic syndrome (MetS) and atherosclerosis. Visceral adiposity (central obesity) plays a more important role in MetS and atherosclerosis^[1] than total body fat, body fat, and has been included into variety of guidelines as a risk factor for cardiovascular diseases (CVD)^[2-3].

Most studies used waist circumference (WC) to define visceral obesity as a brief parameter. It is widely accepted that WC >90 cm for men can predict future CVD events. The International Diabetes Federation (IDF) definition for MetS in 2009 that recommended 80 cm WC in Chinese women for the diagnosis of visceral obesity is not linked with relevant cardiovascular risks and calls for updated evidence^[4]. However, the simple parameter cannot distinguish visceral adiposity from subcutaneous adiposity. CT and MRI are recommended by IDF for the diagnosis of visceral obesity^[4]. Our previous study showed that two or more components of MetS increase with the increasing extent of visceral obesity and the optimal WC cutoff for visceral obesity is 90 cm in men and 85 cm in women, which has been included in the Chinese Joint Committee for Developing Chinese Guideline (JCDCG)^[5]. It has been shown that visceral obesity can predict future diabetes and the cutoff of WC, indicating that visceral obesity in women is near 85 cm^[6]. In addition, a previous prospective study on MetS and cardiovascular events in Shanghai showed that the cutoff of WC we revised is more reliable for predicting future CVD events in Chinese people than the IDF definition^[7].

Carotid intima-media thickness (C-IMT) is independently related with future CVD events and measurement of C-IMT can help improve cardiovascular risk prediction and reclassification^[8]. However, few studies are available on WC and subclinical atherosclerosis in Chinese women. We therefore designed the present study in order to evaluate whether WC ≥ 85 cm can identify potential preclinical atherosclerosis in asymptomatic people.

MATERIALS AND METHODS

Study Subjects

The Shanghai obesity study (SHOS) was a

prospective study aiming to find out the prevalence of MetS and other relating diseases. The study was conducted in 2009-2012 and 4000 individuals with risk factors (such as smoke, hypertension, hyperglycemia, dyslipidemia, and family history) for CVD were divided into observation group ($n=1000$) and control group ($n=3000$). If the incidence of events was 5%-7% in the control group, it was convective (more than 0.8) to detect the risk ratio as 1.5 ($\alpha=0.05$). Actually 5000 individuals were recruited from 4 communities (1250 for each community) in Shanghai, China, in consideration of about 20% dropout rate^[9]. In this study, 2840 women aged ≥20 years were selected from the SHOS. Thirty-eight with liver function (ALT, AST or direct bilirubin >1.5 times the upper limit), 12 with abnormal renal function (serum creatinine >115 $\mu\text{mol/L}$) or on hemodialysis, 178 with hyperthyroidism (TSH <0.3 mIU/L, FT4 >24.5 pmol/L, FT3 >6.3 pmol/L) and hypothyroidism (TSH >4.8 mIU/L, FT4 <10.3 pmol/L), 25 with cancer, 7 with cirrhosis accompanying ascites, 90 with known history of cardiovascular disease, 2 with psychiatric disturbance, 2 on current treatment for systemic corticosteroids, 123 with incomplete anthropometric data or laboratory evaluation were excluded from this study. Finally, 2365 subjects were enrolled in this study. Also a questionnaire of sickness history and drug-taking history was completed by each participant. This study was approved by Ethics Committee of Affiliated Sixth People's Hospital of Shanghai Jiaotong University. All the study subjects signed informed consent form.

Physical Examination and Laboratory Test

All participants underwent physical examination. Their weight, height, blood pressure (BP), and WC were measured. Their BMI was calculated as weight (kilogram) divided by height (meter) square. Their blood pressure was measured 3 times with a sphygmomanometer by one operator at an interval of 3 min and the mean value was recorded. WC was measured with a tape around the abdomen horizontally at the midpoint of the costal margin and the iliac crest on mid-axillary line. A 75 g oral glucose tolerance test was performed once for subjects without diabetes and 100 g carbohydrate (steamed bread meal) was given to diabetic subjects.

Ten-hour fasting blood samples were taken from all participants. Fasting plasma glucose and 2 h-post OGTT plasma glucose was measured using glucose oxidase (Hitachi 7600-120; Roche kit). Glycosylated

hemoglobin A1c (HbA1c) was measured by high-pressure liquid chromatography (Variant II, Bio-Rad Inv., Hercules, CA, USA). Serum TG, TC, LDL-C, and HDL-C were measured with a parallel, multichannel analyzer (Hitachi 7600-120, Tokyo, Japan). C-reactive protein (CRP) was detected by particle-enhanced immunonephelometry (Siemens Healthcare Diagnostic Inc., Newark, USA). Serum fast insulin level was measured by electrochemiluminescence immunoassay (Cobase e411 immunoassay analyzer, Roche Diagnostics GmbH; Roche) for calculating HOMA-IR as $\text{FPG (mmol/L)} \times \text{fast serum insulin (mU/L)} / 22.5$.

Carotid Ultrasonography

Ultrasound doctor blinded to this study scanned both common carotid arteries of all participants with high-resolution B-mode scanner (VOLUSION 730, EXPERT, GE, USA) and scanned carotid artery with a 10.0-MHz probe. C-IMT was measured in the far wall of common carotid arteries in both sides, which was 1 cm proximal to the carotid bulb. C-IMT value was defined as the mean maximal IMT of each carotid artery in both sides^[10].

Diagnostic Criteria

The MetS was diagnosed according to the 2007 Joint Committee for Developing Chinese Guidelines (JCDCG2007), namely the presence of 3 or more of the following components: 1. WC >85 cm for women, 2. serum TC ≥ 1.7 mmol/L or specific treatment for lipid abnormality, 3. HDL-C <1.04 mmol/L or specific treatment for lipid abnormality, 4. blood pressure $\geq 130/85$ mmHg or treatment of previously diagnosed hypertension, 5. FPG ≥ 6.1 mmol/L and/or 2hPG ≥ 7.8 mmol/L or previously diagnosed as type 2 diabetes^[11]. Overweight or obese subjects were defined according to the WHO 1999 criteria as BMI ≥ 25.0 kg/m² and normal weight or lean subjects were defined as BMI <25.0 kg/m²^[12].

Statistical Analysis

SPSS 15.0 was used for all statistical analyses. Normal data were expressed as mean \pm SD for skew values. The abnormal distribution of clinical characteristics in different groups was compared by Mann-Whitney U test. The categorical variables were compared by Chi-square test between groups. The relation between C-IMT and other variables was studied by Spearman correlation analysis. Trend was analyzed by one way ANOVA. The independent relation between WC and C-IMT was analyzed by

multiple stepwise regression analysis. The independent association between different WC categories and elevated C-IMT was studied by Logistic regression analysis. All *P* values were two-tailed and *P*<0.05 was considered significantly different.

RESULTS

Characteristics of Participants

Finally, 2365 women were included in the database (840 premenopausal women and 1525 postmenopausal women) aged 20-77 years (mean 47.8-58.5 years).

The participants were divided into lean or normal weight group and overweight or obese group according to their BMI. Each group was further divided into 2 subgroups according to their WC cutoff defined for abdominal obesity in our previous study.

The characteristics in different subgroups are shown in Table 1, showing that overweight or obese women were older than lean or normal weight women (*P*<0.05). The BMI, WC, blood pressure, plasma glucose, frequency of MetS, serum TG, HDL-C, LDL-C, and CRP levels were significantly higher in overweight or obese group than in lean or normal weight group (*P*<0.01). The number of smokers was greater in overweight or obese group than in lean or normal weight group (*P*<0.01). However, no significant difference was found in TC level between the two groups.

The C-IMT was significantly greater in overweight or obese group than in lean or normal weight group and in those with their WC ≥ 85 cm than in those with their WC <85 cm (*P*<0.05).

Correlation between C-IMT and Anthropometric Parameters, Glucose, Insulin, and Lipid Profile

Spearman correlation analysis showed that the C-IMT was significantly correlated with the variables in Table 2 (*P*<0.01), except HDL-C in premenopausal women and TC in postmenopausal women.

After adjusted for age, BMI, anti-hypertensive, anti-diabetic and lipid-lowering treatment and after logarithm of data, partial correlation analysis showed that the C-IMT was positively correlated with the WC in both premenopausal and postmenopausal women (Table 2, *P*<0.01).

Multiple stepwise regression analysis showed that the WC, BMI, age, blood pressure, HOMA-IR, plasma glucose, lipid profiles, CRP, smoking status, anti-hypertensive therapy, anti-diabetic therapy, and

Table 1. Characteristics of Different Subgroups

Characteristics	Subgroup of Lean/Normal Weight Individuals		Subgroup of Overweight/Obese Individuals	
	All (n=1658)	WC <85 cm (n=1486)	All (n=707)	WC ≥85 cm (n=208)
Age (yr)	53.6 (47.7-58.3)	53.4 (47.3-58.1)	54.1 (48.4-59.1) [#]	54.2 (49.6-59.4) [▲]
Anthropometric measures				
BMI (kg/m ²)	22.1 (20.4-23.5)	21.8 (20.3-23.2)	26.9 (25.8-28.4) ^{###}	27.5 (26.3-29.2) ^{▲▲}
WC (cm)	76.0 (71.0-80.0)	75.0 (70.5-79.0)	88.0 (84.0-92.0) ^{###}	90.0 (87.5-94.0) ^{▲▲}
SBP (mmHg)	120.0 (110.0-129.3)	120.0 (110.0-128.7)	124.7 (116.7-132.7) ^{###}	125.3 (118.7-133.3) [▲]
DBP (mmHg)	76.7 (70.0-80.0)	76.0 (70.0-80.0)	79.3 (71.3-84.7) ^{###}	80.0 (72.0-86.0) [▲]
Blood glucose and insulin				
FBG (mmol/L)	5.22 (4.92-5.57)	5.20 (4.91-5.55)	5.47 (5.13-6.07) ^{###}	5.54 (5.15-6.16) ^{▲▲}
2hPG (mmol/L)	6.44 (5.55-7.69)	6.36 (5.50-7.58)	7.37 (6.23-9.17) ^{###}	7.48 (6.30-9.45) [▲]
HbA1c (%)	5.60 (5.40-5.90)	5.60 (5.40-5.90)	5.80 (5.50-6.10) ^{###}	5.80 (5.60-6.10) [▲]
HOMA-IR	1.63 (1.14-2.29)	1.58 (1.09-2.20)	2.64 (1.90-3.75) ^{###}	2.78 (2.12-4.02) ^{▲▲}
Lipid profiles				
TC (mmol/L)	5.23 (4.59-5.97)	5.21 (4.57-5.97)	5.32 (4.69-5.99)	5.32 (4.69-5.96)
TG (mmol/L)	1.12 (0.79-1.63)	1.09 (0.77-1.56)	1.46 (1.08-2.04) ^{###}	1.53 (1.11-2.13) ^{▲▲}
HDL-C (mmol/L)	1.56 (1.34-1.80)	1.57 (1.35-1.82)	1.39 (1.21-1.59) ^{###}	1.36 (1.19-1.55) ^{▲▲}
LDL-C (mmol/L)	3.22 (2.65-3.80)	3.19 (2.64-3.80)	3.40 (2.90-4.00) ^{###}	3.43 (2.90-4.00)
Inflammatory factor				
CRP (mg/L)	0.53 (0.26-1.09)	0.49 (0.23-1.01)	1.23 (0.64-2.38) ^{###}	1.31 (0.75-2.51) ^{▲▲}
Ultrasound measurement				
C-IMT (mm)	0.59±0.10	0.58±0.10	0.62±0.10 ^{###}	0.62±0.09 ^{▲▲}
History of medication and smoke status				
Anti-hypertensive therapy n (%)	220 (13.3)	171 (11.5)	192 (27.2) ^{###}	146 (29.3)
Anti-diabetic therapy n (%)	40 (2.4)	31 (2.1)	43 (6.1) ^{###}	36 (7.2)
Lipid-lowering therapy n (%)	36 (2.2)	32 (2.2)	27 (3.8) [#]	22 (4.4)
Current smoker n (%)	5 (0.3)	5 (0.3)	10 (1.4) [#]	7 (1.4)
Components of Mets				
Hypertiglyceridemia n (%)	380 (22.9)	313 (21.1)	278 (39.3) ^{###}	211 (42.3) [▲]
Low HDL-C n (%)	76 (4.6)	66 (4.4)	67 (9.5) ^{###}	51 (10.2)
Hypertension n (%)	559 (33.7)	467 (31.4)	386 (54.6) ^{###}	292 (58.5) ^{▲▲}
Hyperglycemia n (%)	432 (26.1)	363 (24.4)	345 (48.8) ^{###}	253 (50.7)
MetS n (%)	162 (9.8)	91 (6.1)	286 (40.5) ^{###}	254 (50.9) ^{▲▲}

Note. Abbreviations: 2hPG: 2-h post-OGTT plasma glucose; BMI: body mass index; C-IMT: carotid intima-media thickness; CRP: C-reactive protein; DBP: diastolic blood pressure; FBG: fasting plasma glucose; HDL-C: high-density lipoprotein cholesterol; HOMA-IR: homeostasis model assessment-insulin resistance; LDL-C: low-density lipoprotein cholesterol; SBP: systolic blood pressure; TC: total cholesterol; TG: total triglyceride; WC: waist circumference; *P<0.01 vs BMI <25.0 kg/m², WC <85 cm; #P<0.05 vs BMI <25.0 kg/m², WC <85 cm; ###P<0.01 vs BMI <25.0 kg/m², WC <85 cm; ▲P<0.05 vs BMI ≥25.0 kg/m², WC <85 cm; ▲▲P<0.01 vs BMI ≥25.0 kg/m², WC <85 cm; ▲▲▲P<0.001 vs BMI ≥25.0 kg/m², WC <85 cm. Data are expressed as mean±SD.

lipid-lowering therapy were the independent risk factors for CVD (Table 3). It can be seen from Table 3 that WC, age, SBP, HOMA-IR, anti-hypertension

therapy, and FPG were the independent risk factors for C-IMT, while the HDL-C was a protective factor for C-IMT.

Table 2. Correlation between C-IMT and Other Variables

Variables	Premenopausal Women				Postmenopausal Women			
	C-IMT (mm) (n=840)		Adjusted (n=840)		C-IMT (mm) (n=1525)		Adjusted (n=1525)	
	r	P	r	P	r	P	r	P
Age (yr)	0.347	<0.001	/	/	0.229	<0.001	/	/
BMI (kg/m ²)	0.242	<0.001	/	/	0.148	<0.001	/	/
WC (cm)	0.281	<0.001	0.104	0.003	0.157	<0.001	0.063	0.013
SBP (mmHg)	0.318	<0.001	0.178	<0.001	0.238	<0.001	0.176	<0.001
DBP (mmHg)	0.242	<0.001	0.175	<0.001	0.151	<0.001	0.116	<0.001
FPG (mmol/L)	0.266	<0.001	0.106	0.002	0.163	<0.001	0.109	<0.001
2hPG (mmol/L)	0.124	<0.001	0.042	0.221	0.120	<0.001	0.069	0.007
HbA1c (%)	0.117	0.001	0.006	0.860	0.090	<0.001	0.066	0.010
TC (mmol/L)	0.140	<0.001	0.058	0.091	0.045	0.079	0.041	0.110
TG (mmol/L)	0.125	<0.001	0.037	0.282	0.102	<0.001	0.039	0.128
HDL-C (mmol/L)	-0.058	0.094	-0.004	0.916	-0.108	<0.001	-0.078	0.002
LDL-C (mmol/L)	0.244	<0.001	0.142	<0.001	0.095	<0.001	0.107	<0.001
CRP (mg/L)	0.156	<0.001	0.042	0.223	0.124	<0.001	0.026	0.307
HOMA-IR	0.297	<0.001	0.214	<0.001	0.170	<0.001	0.082	0.001

Note. Abbreviations: 2hPG: 2-h post-OGTT plasma glucose; BMI: body mass index; C-IMT: carotid intima-media thickness; CRP: C-reactive protein; DBP: diastolic blood pressure; FPG: fasting plasma glucose; HDL-C: high-density lipoprotein cholesterol; HOMA-IR: homeostasis model assessment-insulin resistance; LDL-C: low-density lipoprotein cholesterol; SBP: systolic blood pressure; TC: total cholesterol; TG: total triglyceride; WC: waist circumference. Partial correlation analysis adjusted for age, BMI, anti-hypertensive, anti-diabetic, and lipid-lowering treatment. Data are expressed as logarithm.

Table 3. Stepwise Multiple Linear Regression Analysis of C-IMT

Independent Variables	β	SEM	Standardized β	P
Age (yr)	0.003	<0.001	0.327	<0.001
SBP (mmHg)	0.001	<0.001	0.134	<0.001
HOMA-IR	0.004	0.002	0.057	0.014
LDL-C (mmol/L)	0.008	0.001	0.097	<0.001
Anti-hypertension therapy	0.021	0.005	0.008	<0.001
WC (cm)	0.106	0.043	0.054	0.014
FPG (mmol/L)	0.006	0.002	0.064	0.006
HDL-C (mmol/L)	-0.012	0.006	-0.042	0.036

Note. Abbreviations: FPG: fasting plasma glucose; HDL-C: high-density lipoprotein cholesterol; HOMA-IR: homeostasis model assessment-insulin resistance; LDL-C: low-density lipoprotein cholesterol; SBP: systolic blood pressure; WC: waist circumference. Variables included were age, BMI, WC, SBP, DBP, FPG, 2hPG, HbA1c, TG, LDL-C, HDL-C, CRP, HOMA-IR, anti-hypertensive therapy, anti-diabetic therapy, lipid-lowering therapy, smoke status and menopausal status.

Relation between WC and C-IMT in Different WC Categories

In order to observe the relation between WC values and C-IMT, the participants ($n=2365$) were divided by WC 5 cm for each subgroup from 70 cm to 90 cm. The C-IMT increased significantly with the increasing WC and reached to a platform in about 85 cm. The greater the WC was, the thicker the carotid intima-media was (Figure 1, $P<0.01$).

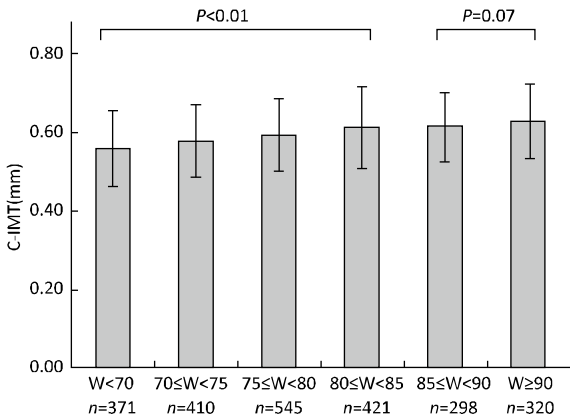


Figure 1. Relation between C-IMT and WC in different WC categories. An increment tendency could be observed in the subgroup with its WC <85 cm ($P<0.01$) while no significant tendency could be found in the subgroup with its WC ≥ 85 cm (Figure 1, $P=0.07$).

A logistic regression model was established in the present study to reveal the independent association between different WC categories and the elevated C-IMT. Women were divided into 3 subgroups according to their WC cutoff of 80 cm and 85 cm. The odd ratio of WC ≥ 80 cm, ≥ 80 cm and <85 cm, ≥ 85 cm for evaluating the risk of C-IMT elevation was 1.632, 1.501, and 1.878, respectively.

DISCUSSION

It is widely convinced that obesity can lead to CVD events^[13]. MetS is a complex cluster of metabolism disorders, known as the risk factor for CVD. Visceral obesity is considered as a fundamental pathology for MetS and is mainly associated with increased risk of cardiovascular morbidity and mortality. Visceral fat area (VFA) ≥ 80 cm² is suitable for diagnosing 2 or more components of MetS^[5]. C-IMT is used as a subclinical indicator for

atherosclerosis. The association between C-IMT and CVD events was first described in 1993^[14]. Since then, more studies have focused on C-IMT in order to find out its independent effect on myocardial infarction, stroke and coronary arterial disease. It was reported that the risk of CVD events increases with the increasing C-IMT (RR increases approximately 15% per 0.10 mm of C-IMT)^[15]. It has been shown that the C-IMT is significantly greater in patients with MetS than in those without MetS^[16]. It was reported that abdominal obesity is positively correlated with C-IMT^[17]. CT, MRI, BMI, and WC are commonly used to assess abdominal obesity. Although CT or MRI is the standard method recommended by IDF for assessing abdominal obesity, they are limited for wide application due to their cost. Visceral fat area ≥ 80 cm² could identify subclinical carotid atherosclerosis^[10]. In this study, the WC was found to be positively related with C-IMT and one of the independent risk factors for C-IMT, indicating that WC ≥ 85 cm can identify subclinical atherosclerosis.

It has been shown that menopause exerts an independent effect on fat mass and visceral obesity after the withdrawal of estrogen^[18]. Similarly in our study, the BMI, WC and frequency of visceral obesity were higher in postmenopausal women than in premenopausal individuals. However, the correlation and regression analysis showed no difference even after adjusting the menopausal status. Whether menopause leads to subclinical atherosclerosis remains unknown and needs further consideration.

It was reported that WC can predict future C-IMT increment and even the formation of carotid plaques but cannot find out any optimal cutoff^[19]. A Korean study has defined 84 cm as the optimal WC cutoff in women, which is well correlated with MetS^[20]. A high WC seems to be associated with carotid atherosclerotic burden and WC >86.5 cm in elderly women can be defined as a marker of future cardiovascular events^[21-22]. A Japanese study in 2011 demonstrated that the optimal cutoff of WC in detecting cardiovascular risk factors in Japanese women is near 82 cm^[23], which is consistent with the optimal cutoff of WC of 82.3 cm^[24]. Interestingly, the cutoff of WC in East Asia seems to be unified. In the present study, WC was significantly correlated with C-IMT, and WC was as significant as VFA in identifying subclinical atherosclerosis, indicating that the patients should be aware of cardiovascular diseases if their WC is ≥ 85 cm.

With regard to the relation between WC and CVD events, the working group on obesity in China (WGOC) checked out the epidemiological data about 240 000 people^[25-26]. It was reported that those with their BMI >24 kg/m² are more likely to develop hypertension and diabetes than those with normal BMI. Moreover, the prevalence of more than two risk factors, such as hypertension, hyperglycemia, high total cholesterol, hypertriglyceridemia, low and high density-lipoprotein cholesterol, in people with exceeding BMI is 3-4 times higher than in those with normal BMI. These risk factors are also found in about 90% of the people with their BMI >28 kg/m². Women with their WC >80 cm are more likely to develop diabetes and hypertension. The prevalence of more than 2 risk factors in women with their WC ≥80 cm is 4 times higher than in those with normal WC. Therefore, the WGOC defined the BMI cutoff of 24 kg/cm² and 28 kg/cm² for overweight and obesity, respectively. The WC cutoff was set as 80 cm for central obesity in women. The above risk factors may eventually lead to atherosclerosis. C-IMT is usually used to describe the extent of atherosclerosis. However, few studies are available on the relation between WC and C-IMT in Chinese women. In the present study, the WC was independently correlated with subclinical carotid atherosclerosis and WC was correlated with C-IMT. Further prospective epidemiological survey is still needed in order to verify which cutoff of WC is more predictable for subclinical carotid atherosclerosis.

This study has certain limitations. First, it was an observational study. Second, the age of subjects included in this study was not distributed in an average level.

In conclusion, WC is significantly correlated with C-IMT in Chinese women and is an independent risk factor for C-IMT. WC ≥85 cm can be used to identify the risk factors for subclinical carotid atherosclerosis in women of Shanghai, China.

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DECLARATION OF INTEREST

The authors declare no conflict of interest.

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