Original Article

Relationship between Waist Circumference and Elevation of Carotid Intima-media Thickness in Newly-diagnosed Diabetic Patients*

ZHANG Lei, SHEN Yun, ZHOU Jian, PAN Jie Min, YU Hao Yong, CHEN Hai Bing, LI Qing, LI Ming, BAO Yu Qian#, and JIA Wei Ping#

Department of Endocrinology and Metabolism, Sixth People's Hospital Affiliated to Shanghai Jiao Tong University; Shanghai Clinical Center for Diabetes; Shanghai Diabetes Institute; Shanghai Key Laboratory of Diabetes Mellitus; Shanghai 200233, China

Abstract

Objective Waist circumference, as a brief indicator of visceral obesity, is associated with multi-metabolic disorders and cardiovascular diseases. The present study was aimed to find out the relationship between waist circumference and carotid intima media thickness (C-IMT), as well as the best waist circumference cutoff for identifying C-IMT elevation in Chinese male patients with newly-diagnosed diabetes.

Methods Five hundred and seventy-eight patients from Department of Endocrinology and Metabolism in Shanghai Sixth People's Hospital affiliated to Shanghai Jiao Tong University were enrolled. Both physical examination (for measurement of waist circumference) and carotid ultrasonography (for measurement of C-IMT) were performed.

Results After grouping according to the quartiles of C-IMT, the waist circumference increased across all its quartiles. The waist circumference in 3rd and 4th quartiles (90.7±9.8 cm and 90.8±9.6 cm) was significant higher than in 1st and 2nd quartiles (P<0.05). When subjects were divided into 4 groups according to waist circumference, the C-IMT of subjects with waist circumference 90-95 cm was significant higher than that of subjects with waist circumference 85-90 cm and less than 85 cm respectively (P<0.05). Both spearman and partial correlation analysis showed that C-IMT was positively correlated with waist circumference (P<0.01). C-IMT was found significantly elevated with the increase of waist circumference. Multiple stepwise regression analysis showed that waist circumference was one of the independent risk factors of C-IMT. After an average of 2.23±0.85 years follow up, there was a significant elevation of C-IMT in the group with baseline waist circumference over 90 cm P<0.05), while no significant difference was detected in the group with baseline waist circumference less than 90 cm (P=0.27). Logistic regression showed that baseline waist circumference over 90 cm was associated with a relative risk to C-IMT elevation of 1.132 (95% CI 1.043-1.431, P<0.05).

Conclusion Among newly-diagnosed diabetic male patients, waist circumference over 90 cm not only reflects sub-clinical atherosclerosis in early stage, but also predicts the progression of atherosclerosis.

Key words: Waist circumference; Carotid intima media thickness; Metabolic syndrome

Biomed Environ Sci, 2014; 27(5): 335-342 doi: 10.3967/bes2014.058 ISSN: 0895-3988

www.besjournal.com (full text) CN: 11-2816/Q

*This work was funded by National Key Technology R&D Program of China (2012BAI02B03) and Key Discipline of Public Health of Shanghai (Epidemiology) (12GWZX0104).

#Correspondence should be addressed to BAO Yu Qian and JIA Wei Ping. Tel: 86-21-64369181, Fax: 86-21-64368031, E-mail: byq522@163.com; wpjia@sjtu.edu.cn

Biographical note of the first author: ZHANG Lei, male, born in 1978, MD, majoring in endocrinology and metabolism.

Received: September 5, 2013; Accepted: December 15, 2013

INTRODUCTION

Obesity has become a worldwide health problem. As estimated by the World Health Organization (WHO), overweight individuals will reach 2.3 billion by 2015 with 700 million obese ones[1]. It is widely convinced that obesity is contributed to a wealth of metabolic disorders, among which the closest are hypertension, hyperglycemia and dyslipidemia[2]. Metabolic syndrome (MS) is defined as visceral obesity combined with the above mentioned disorders. A cluster of multi-metabolic disorders may finally lead to future cardiovascular events, threatening the health of the mankind[3]. Waist circumference is now widely used as a brief indicator for assessment of visceral obesity. The Working Group on Obesity in China (WGOC) has analyzed more than 240 000 domestic personal data and found that people with exceeding waist circumference were more likely to suffer diabetes and hypertension than those with normal waist circumference. The risk was even 4 times higher. So the WGOC has defined an optimal waist circumference cutoff for men in identifying visceral obesity according to all the epidemiological data, which is more than 85 cm[4-5]. In our study group, we found that when applying visceral fat area (VFA) as the precise index, 80 cm^2 was an optimal cutoff for identifying visceral obesity and its corresponding waist circumference was 90 cm[6]. The result mentioned was also been included in the 2007 Joint Committee for Developing Chinese Guidelines (JCDCG2007) definition[7]. Furthermore, a 7.8-year follow up study was also conducted, which identified that waist circumference of 88 cm was significant in predicting future diabetes[8].

Atherosclerosis is the main pathological process of cardiovascular diseases (CVD). Increment of carotid intima media thickness (C-IMT) is an early phase of atherosclerosis, which is also a strong predictive factor of future CVD events[9]. No previous study has ever been published about the relationship between waist circumference and C-IMT in the Chinese male population. Therefore, the present study was aimed to focus on the relationship in question and to find out the optimal cutoff for identifying C-IMT elevation.

MATERIALS AND METHODS

Study Subjects

Actually five hundred and seventy-eight newly diagnosed diabetic individuals were recruited from Department of Endocrinology and Metabolism, Shanghai Sixth People's Hospital affiliated to Shanghai Jiao Tong University. We excluded individuals according to the following criterion: abnormal liver function (alanine aminotransferase (ALT), aspartate transaminase (AST) or direct bilirubin >1.5 times the upper limit of normal); renal dysfunction [serum creatinine (Scr) >115 μmol/L] or patients under hemodialysis; hyperthyroidism and hypothyroidism; presence of cancer; cirrhosis with ascites; psychiatric disturbance; pregnancy; current treatment with systemic corticosteroids; incomplete anthropometric data or laboratory evaluation. Eventually, 578 participants were qualified in this study. Also a questionnaire of medical history and medicine-taking history was accessible for each subject. This study was approved by Ethics Committee of Sixth People's Hospital affiliated to Shanghai JiaoTong University. Informed consents were obtained from all the subjects.

Physical Examination and Laboratory Information

All subjects received physical examinations, including measurement of weight, height, waist circumference and blood pressure (BP). The body mass index (BMI, kg/m^2) was defined as weight (kilogram) divided by height (meter) square. Waist circumference was measured via a tape going around the abdomen horizontally at the midpoint of the costal margin and the iliac crest on mid-axillary line. Blood pressure was measured by means of a sphygmomanometer.

Blood samples were all collected from participants in a 10 h fast status in the morning. Fast plasma glucose (FPG) was measured by glucose oxidase method (Hitachi 7600-120; Roche kit). Glycated hemoglobin A1c (HbA1c) was detected via high-pressure liquid chromatography (Variant II, Bio-Rad Inv., Hercules, CA, USA). ALT, AST, Scr, uric acid (UA) were assessed by enzymatic method with an automatic biochemical analyzer (7600-020, Hitachi Inc., Tokyo, Japan). Lipid profiles including serum low-density lipoprotein cholesterol (LDL-C, direct assay method, Sekisui Medical Co. Ltd., Tokyo, Japan), high-density lipoprotein cholesterol (HDL-C, direct assay method, Sekisui Medical Co. Ltd., Tokyo, Japan), serum triglyceride (TG, enzymatic procedures, Roche Diagnostics GmbH, Mannheim, Germany), serum total cholesterol (TC, enzymatic procedures, Roche Diagnostics GmbH, Mannheim, Germany) was detected on a parallel, multichannel analyzer

(7600-020, Hitachi Inc., Tokyo, Japan). C-reaction protein (CRP) was measured by particle-enhanced immuno-nephelometry (Siemens Healthcare Diagnostic Inc., Newark, USA) and serum fast C peptide (FCp) level was assayed by electrochemiluminescence immunoassay (cobase e411 immunoassay analyzer, Roche Diagnostics GmbH; Roche). Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated by using HOMA2 model Calculator software from the Oxford Center for Diabetes, Endocrinology and Metabolism.

Carotid Ultrasonic Measurement

A high-resolution B-mode scanner (VOLUSION 730, EXPERT, GE, USA) and a 10.0-MHz probe was used for carotid artery scanning. An ultrasonography operator blinded to this study did the scanning of both common carotid arteries. 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 of the maximal IMT of each carotid artery in both sides.

Diagnostic Criteria

The 2007 Joint Committee for Developing Chinese Guidelines (JCDCG2007) definition was applied as MS criteria[7], which was the presence of three or more of the following components: 1. Abdominal obesity: waist circumference over 90 cm for men; 2. TG≥1.7 mmol/L or specific treatment for lipid abnormality; 3. HDL-C<1.04 mmol/L or specific treatment for lipid abnormality; 4. BP≥130/85 mmHg or treatment of previously diagnosed hypertension; 5. FPG≥6.1 mmol/L and/or 2-h postprandial plasma glucose (2hPG)≥7.8 mmol/L or previously diagnosed type 2 diabetes. Diabetes was also defined according to WHO 1999 criteria[10] as FPG of at least 7.0 mmol/L and/or 2h PG of at least 11.1 mmol/L.

Statistical Analysis

We used SPSS 15.0 for all statistical analysis. Normal data were described as mean±standard deviation and median (inter-quartile range) for skew values. Mann-Whitney U test was applied for all skew clinical characteristics to do the comparison among groups. Concerning categorical variables, chi-test was applied in comparison between groups. Receiver operating characteristic (ROC) analysis was conducted to look for the optimal cutoff of waist circumference to represent elevated C-IMT. Spearman and partial correlation analysis was performed to explore the relation between C-IMT and other variables. One way ANOVA was used for trend analysis. Multiple stepwise regression analysis was used to demonstrate the independent relation between waist circumference and C-IMT. Logistic regression analysis was performed to show the independent association between different waist circumference categories and the elevation of C-IMT. All P values were two-tailed and considered statistically significant for less than 0.05.

RESULTS

Five hundred and seventy eight participants were finally recruited into the study with an average age of 51.4±12.9 years (from 21 to 83 years old). The average duration of diabetes was 8 months (from 10 days to 2 years). The average C-IMT value of the whole study population was 0.77±0.17 mm.

All the subjects were divided into 4 groups according to the quartiles of C-IMT (<0.65 mm, 0.65-0.75 mm, 0.75-0.80 mm, >0.80 mm) .The waist circumference increased across its quartiles (87.4±9.0 cm, 88.2±9.2 cm, 90.7±9.8 cm and 90.8±9.6 cm in 1st, 2nd, 3rd, and 4th quartiles of waist circumference distribution, respectively). The waist circumference in 3rd and 4th quartiles was significant higher than in 1st and 2nd quartiles (P<0.05). Between 3rd, and 4th quartiles, there were no significant differences in waist circumference (P>0.05). Therefore, after the data from 3rd and 4th were pooled, the waist circumference in 3rd+4th quartiles was 90.7±9.7 cm. To verify the cut-off value of waist circumference for elevated C-IMT, ROC curve analysis was performed. By maximizing the Youden index, 90 cm was selected as optimal cutoff of waist circumference, which represented a sensitivity of 50.3% and a specificity of 61.3%. At this level, the Youden Index was 0.117, which was higher than waist circumference over 85 cm and waist circumference over 95 cm (Youden Index 0.068 and 0.056, respectively).

To investigate whether the cut-off value of waist circumference (90 cm) was effective to detect elevation of C-IMT, the patients were divided into 4 groups according to waist circumference (Group A: waist circumference ≤85 cm, Group B: 85 cm < waist circumference ≤90 cm, Group C: 90 cm < waist circumference ≤95 cm, Group D: waist circumference >95 cm). The clinical characteristics were shown in Table 1. As the waist circumference rose, the level of

BMI, systolic BP (SBP), diastolic BP (DBP), ALT, AST, TG, UA, FPG, FCP, HOMA-IR, CRP increased, but HDL-C and HbA1c decreased (all *P* trend <0.05). There was no difference in age, smoking status and Scr among these 4 groups (all *P*>0.05). The proportions of dyslipidemia, hypertension and MS also ascended with waist circumference (all *P* trend <0.05). There were significant differences in BMI, ALT, AST, HDL-C, FCp, HOMA-IR (all *P*<0.05) between group B and group C. The C-IMT was 0.74±0.16, 0.76±0.18, 0.80±0.16, 0.79±0.17 respectively in patients stratified by waist circumference category. The C-IMT in group C was significant higher than in group B and group A (*P*<0.05).

A spearman correlation analysis was then performed. Significant positive correlations of C-IMT with waist circumference were found (*r*=0.145, *P*<0.01, Table 2). After adjustment for age, BMI, BP, HOMA-IR, FPG, liver function, UA, lipid profiles and CRP, partial correlation analysis showed that C-IMT was still positively correlated with waist circumference (*r*=0.108, *P*<0.01).

Table 1. Characteristics of Subjects in Different Waist Circumference Groups

Items	A	B	C	D
n	183	131	109	155
Age (yr)	50.7±12.8	52.5±12.1	52.1±12.5	51.0±13.8
Smoking (%)	35.7	43.6	37.8	40.0
BMI (kg/m^2)	22.0±2.3	24.4±2.4*	26.0±1.9$^{*\#}$	29.0±3.3$^{*\#\blacktriangle}$
SBP (mmHg)	122±14	125±14	127±15*	129±16$^{*\#}$
DBP (mmHg)	78±9	80±9*	81±10*	82±10*
ALT (U/L)	22.5±16.6	27.6±20.4*	34.0±24.0$^{*\#}$	38.3±26.6$^{*\#}$
AST (U/L)	21.0±11.1	22.8±12.7	25.7±12.7$^{*\#}$	28.6±15.7$^{*\#\blacktriangle}$
TC (mmol/L)	4.55±1.01	4.70±1.02	4.83±1.09*	4.70±1.24
TG (mmol/L)	1.40±1.06	1.95±1.54*	2.01±1.25*	2.42±1.63$^{*\#\blacktriangle}$
HDL-C (mmol/L)	1.16±0.35	1.03±0.28*	0.97±0.20$^{*\#}$	0.94±0.26$^{*\#}$
LDL-C (mmol/L)	3.04±0.91	3.23±0.98*	3.32±0.93*	3.01±0.95$^{\#\blacktriangle}$
Cr (μmol/L)	72.5±20.2	73.9±15.2	76.6±23.6	75.9±19.8
UA (μmol/L)	304±79	333±86*	347±79*	370±83$^{*\#\blacktriangle}$
FPG (mmol/L)	7.66±2.64	8.42±2.82*	8.42±2.86*	8.88±3.36*
HbA1c (%)	9.80±2.84	9.48±2.71	8.95±2.30*	9.09±2.42*
FCp (ng/mL)	1.36±0.91	1.83±0.89*	2.21±1.08$^{*\#}$	2.52±1.05$^{*\#\blacktriangle}$
HOMA-IR	1.13±0.76	1.59±0.80*	1.90±0.94$^{*\#}$	2.23±0.97$^{*\#\blacktriangle}$
CRP (mg/L)	0.69	1.03 (0.49-2.03)	1.06 (0.5-2.35)	1.60$^{*\#\blacktriangle}$ (0.82-3.78)
C-IMT (mm)	0.74±0.16	0.76±0.18	0.80±0.16$^{*\#}$	0.79±0.17$^{*\#}$
Hypertriglyceridemia *n* (%)	49 (26.8)	54 (41.2)*	56 (51.4)$^{*\#}$	97 (62.6)$^{*\#\blacktriangle}$
Low HDL-C *n* (%)	80 (43.7)	80 (61.1)*	80 (73.4)$^{*\#}$	116 (74.8)$^{*\#}$
Hypertension *n* (%)	59 (32.2)	61 (46.6)*	53 (48.6)*	95 (61.3)$^{*\#\blacktriangle}$
MS *n* (%)	49 (26.8)	67 (51.1)*	68 (62.4)$^{*\#}$	113 (72.9)$^{*\#\blacktriangle}$

Note. **P*<0.05 versus Group A, $^{\#}$*P*<0.05 versus Group B, $^{\blacktriangle}$*P*<0.05 versus Group C. All the data in Table 1 were at baseline.

To further detect the relation between waist circumference and C-IMT, multiple stepwise regression analysis was performed (Table 3). Waist circumference, BMI and the basic CVD risk factors including age, blood pressure, HOMA-IR, plasma glucose, liver function, uric acid, lipid profiles, CRP, and smoking status were set as independent variables. As could be seen from Table 3, waist circumference, as well as age, SBP and LDL-C, were independent risk factors for C-IMT.

Table 2. Correlation Analysis with C-IMT

Variables	C-IMT		Adjusted	
	R	*P*	*R*	*P*
Age	0.552	<0.001	/	/
BMI	0.097	0.006	/	/
Waist Circumference	0.145	<0.001	0.123	0.007
SBP	0.194	<0.001	0.178	0.003
DBP	0.056	0.115	0.032	0.218
ALT	-0.043	0.230	-0.004	0.326
AST	-0.007	0.437	-0.001	0.631
FPG	0.018	0.311	-0.003	0.467
HbA1c	0.035	0.333	0.013	0.427
TC	0.047	0.182	0.039	0.216
TG	0.038	0.283	0.006	0.483
HDL-C	-0.016	0.256	-0.004	0.303
LDL-C	0.181	0.014	0.131	0.022
Cr	0.145	<0.001	0.007	0.274
UA	0.089	0.016	0.028	0.152
CRP	0.113	0.003	0.046	0.177
FCp	0.034	0.335	0.023	0.448
HOMA-IR	0.029	0.405	0.016	0.523

Note. Partial correlation analysis adjusted for age, BMI.

Table 3. Multiple Stepwise Regression Analysis

Independent Variables	B	SEM	Standardized β	*P*
Age	0.006	0.001	0.473	0.01
Waist Circumference	0.002	0.001	0.138	0.02
SBP	0.001	0.001	0.136	0.03
LDL-C	0.019	0.007	0.101	0.03

Note. Waist circumference, BMI and the basic CVD risk factors including age, BP, HOMA-IR, FPG, liver function, UA, lipid profiles, CRP, smoking status were included in the model.

To explore the relationship between waist circumference and C-IMT, all the participants were divided into subgroups by 5 cm of waist circumference from 80 cm to 100 cm for each subgroup. A bar graph was then drawn for illustration as was presented in Figure 1, from which we could see generally that the greater waist circumference, the thicker carotid intima-media (*P* for trend <0.01). C-IMT was also significantly elevated with the increase of waist circumference, and reached to a platform in about 90 cm.

Among 578 subjects, 231 had follow up data of at least 1 year. The average follow up period of time was 2.23±0.58 years. These subjects were divided into 2 groups according to the value of waist circumference. Group 1 was defined as waist circumference less than 90 cm (*n*=138), while Group 2 was defined as waist circumference over 90 cm (*n*=93). As shown in Table 4, there was a significant elevation of C-IMT in Group 2 (0.83±0.17 mm *vs*. 0.80±0.16 mm, *P*=0.03), while no significant difference was detected in Group 1 (0.75±0.17 mm *vs*. 0.74±0.16 mm, *P*=0.27). Further logistic regression analysis was conducted by setting elevation of C-IMT as a dependent variable; after adjusting for baseline FPG, HbA1c, BP, CRP, TC, TG, LDL-C, and HDL-C, the baseline waist circumference over 90 cm in men was a risk factor associated with elevation of C-IMT, and the odds ratios was 1.13 (*P*=0.04, 95% CI 1.04-1.43).

DISSCUSSION

The relationship between visceral obesity and CVD events is attributed to the influence of multi-metabolic disorders, which is confirmed by abundant

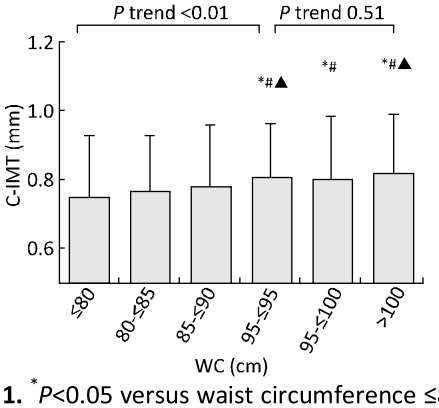

Figure 1. *P<0.05 versus waist circumference ≤80 cm, #P<0.05 versus waist circumference 80-85 cm, ▲P<0.05 versus waist circumference 85-90 cm, *P* trend (overall) <0.01.

prospective studies[11-12]. In recent years, connections among visceral obesity, atherosclerosis and CVD events are paid more attention. C-IMT, studied in this paper, is a predictive indicator for the extent of sub-clinical atherosclerosis. The American Heart Association has declared in his guidelines that increased C-IMT can lead to future CVD events and the relevant risks can also be mitigated by regular follow up of C-IMT[3]. Therefore, to some extent, C-IMT can predict the occurrence of future CVD events. In addition to the brief indices for assessment of visceral obesity mentioned above, the International Diabetes Federation also recommends using computed tomography (CT) or magnetic resonance imaging (MRI) to measure visceral fat area (VFA) as a precise indicator for visceral obesity[13]. In our previous study, VFA was confirmed to be associated with C-IMT and VFA over 80 cm^2 was significantly correlated to the elevation of C-IMT[6]. Compared to total body fat content, accumulation of visceral fat tissue was more effective in reflecting sub-clinical atherosclerosis. However, these precise methods have limited utility owing to the high cost and the complicated operation. Measurement of waist circumference is widely applied in epidemiological investigation. Previously, WGOC has defined a cutoff of waist circumference for visceral obesity in men population via analysis of relevant data, which was 85 cm[4-5]. Nevertheless, our previous study found waist circumference of 90 cm in men population more proper to identify the accumulation of visceral fat[14]. In this study, we focused on waist circumference and the predictive effect of 90 cm for sub-clinical atherosclerosis. We found the independent relationship between waist circumference and C-IMT, as well as the fact that elevation of C-IMT could be accompanied by waist circumference over 90 cm. The result is clinically highly valuable in early screening of atherosclerosis. Concerning the relationship between waist circumference and C-IMT, a 4-year prospective Finnish study in 2001 clarified that waist circumference was associated with accelerated progression of carotid atherosclerosis and waist circumference was defined as an important risk factor for atherosclerosis[15]. In our study, the 2-year follow up data also showed that people with waist circumference over 90 cm had a more significant elevation of C-IMT, which hinted that this cutoff was optimal for reflecting the process of atherosclerosis.

In our previous studies, we revealed a positive relationship between waist circumference and C-IMT in a community-based women population and found that waist circumference over 85 cm for women might be proper in identifying the risk of subclinical atherosclerosis[16]. In order to make up for the lacking information in men population, we found in this study that the optimal cutoff of waist circumference for men was 90 cm by ROC analysis with a respective sensitivity and specificity of 50.3% and 61.3%. The results also hinted that waist

Table 4. Comparison of Clinical Characteristics between Baseline Group and Follow-up Group

Items	Group 1 (Baseline waist circumference less than 90 cm)			Group 2 (Baseline waist circumference over 90 cm)		
	Baseline	Follow-up	*P*	Baseline	Follow-up	*P*
BMI(kg/m^2)	22.3±3.1	22.5±3.2	0.62	26.8±3.0	27.1±3.2	0.67
SBP(mmHg)	123±14	122±12	0.75	127±15	127±12	0.92
DBP(mmHg)	78±10	77±8	0.51	83±10	80±8	0.15
Anti-hypertensive therapy n(%)	31 (22.4)	34 (24.6)	0.81	37 (39.8)	41 (44.1)	0.48
TC(mmol/L)	4.67±1.1	4.28±1.09	0.04	4.66±1.27	4.71±1.16	0.75
TG(mmol/L)	1.65±1.67	1.48±1.12	0.24	2.52±2.54	2.57±2.66	0.83
HDL-C(mmol/L)	1.21±.41	1.27±.44	0.03	1.01±0.39	1.01±0.38	0.99
LDL-C(mmol/L)	3.03±1.03	2.76±.95	0.01	2.87±0.92	2.98±0.87	0.23
Lipid-lowing therapy n(%)	14 (10.1)	23 (16.7)	0.01	11 (11.8)	21 (22.3)	0.01
FPG(mmol/L)	8.48±2.13	7.69±2.1	0.02	9.53±2.42	8.64±1.98	0.03
HbA1c(%)	9.89±1.71	8.46±1.57	0.01	8.82±1.86	8.28±1.88	0.02
C-IMT(mm)	0.74±0.16	0.75±0.17	0.27	0.80±0.16	0.83±0.17	0.03

circumference, as a brief indicator of abdominal obesity could be used as a tool for early screening of cardiovascular risks with high cost effectiveness. Waist circumference was thought possible to represent carotid ultrasonography in early screening of cardiovascular risks.

There are some ethnic and racial differences in waist circumference[17]. Within the whole Asia, Khalil, et al. found that waist circumference could predict the formation of carotid plaque by means of a prospective study[18]. Han, et al. have defined an optimal waist circumference cutoff of 88.1 cm to identify metabolic syndrome in Korean men[19]. Additionally, Seo, et al. focused on the elderly (over 63 years old) and found that the optimal cutoff for metabolic syndrome should be 86.5 cm[20]. In Japan, Nakumura, et al. defined waist circumference of 88 cm as the cutoff for metabolic syndrome in men[21]. When comparing among all the waist circumference cutoffs mentioned with our own findings, the cutoff of the whole East Asia tends to be unified. Our results suggest that men population with waist circumference over 90 cm should pay more attention to their blood glucose, blood pressure, lipid profile, as well as the occurrence of CVD events.

Visceral obesity shares its physiopathologic mechanism with atherosclerosis, including insulin resistance, oxidative stress and involvement of inflammatory factors or cytokines[22]. Responded hyperinsulinemia derived by insulin resistance can influence the function of vascular endothelial cells, thus causing oxidative stress. Consequently, the ability of endothelial cells to produce nitric oxide reduces dramatically and endothelial cells may be severely hurt. Inflammatory factors and cytokines are involved in this process[23]. Abdominal obesity is the risk factor of many other metabolic disorders such as hyperglycemia, dyslipidemia, and hypertension. The accumulation of visceral adiposity can lead to an increment of free fatty acid, thus promoting the degree of insulin resistance and then having a positive function of C-IMT[24]. The detailed mechanism warrants further study in the future.

The subjects enrolled in this study were all newly-diagnosed diabetic patients with an average duration of no more than 2 years. Atherosclerosis is a chronic condition and demands long accumulation of time. It really costs much time for people without metabolic disorders to develop atherosclerosis, so those with a high risk to metabolic disorders are more suitable to be enrolled in this study. The variance of C-IMT in this population might be noticeably changed in the follow-up years. If the study population was selected from the community, the follow-up year might be longer for significant change of C-IMT. Furthermore, body fat distribution was known to be influenced by gender. Body fat distribution was also different between different menopausal statuses in women because of the withdrawal of estrogen. Our data only focused men population here and will be expanded to enroll the whole community-based population in the future.

There are still some limitations. First, the study population enrolled is relatively limited. Secondly, this cross-sectional study cannot tell the exact causal relationship between waist circumference and C-IMT. Finally, the sample size is relatively small.

In conclusion, among newly-diagnosed diabetic men patients, waist circumference over 90 cm not only reflects sub-clinical atherosclerosis in early stage, but also predicts the progression of atherosclerosis.

ACKNOWLEDGEMENTS

Contributors: BAO Yu Qian and JIA Wei Ping conceived and designed the study. ZHANG Lei, SHEN Yun, ZHOU Jian, PAN Jie Min, YU Hao Yong, CHEN Hai Bing, LI Qing, LI Ming recruited samples. ZHANG Lei did the statistical analyses. ZHANG Lei and SHEN Yun wrote the first draft of the paper. ZHANG Lei, SHEN Yun, BAO Yu Qian, and JIA Wei Ping revised the paper and contributed to discussion. ZHOU Jian, PAN Jie Min, YU Hao Yong, CHEN Hai Bing, LI Qing, LI Ming provided the technical support. BAO Yu Qian and JIA Wei Ping shared the correspondence.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCE

1. World Gastroenterology Organization. World Gastroenterology Organization global guidelines on obesity. J Clin Gastroenterol, 2012; 46, 555-61.
2. Eckel RH, Grundy SM, and Zimmet PZ. The metabolic syndrome. Lancet, 2005; 365, 1415-28.
3. 2010 ACCF/AHA Guideline for Assessment of Cardiovascular Risk in Asymptomatic Adults: A Report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation, 2010; 122, e584-e636.

4. Zhou BF. Cooperative Meta-Analysis Group of the Working Group on Obesity in China. Predictive values of body mass index and waist circumference for risk factors of certain related diseases in Chinese adults-study on optimal cut-off points of body mass index and waist circumference in Chinese adults. Biomed Environ Sci, 2002; 15, 83-96.
5. Zhou BF. Effect of body mass index on all-cause mortality and incidence of cardiovascular diseases-report for meta-analysis of prospective studies on optimal cut-off points of body mass index in Chinese adults. Biomed Environ Sci, 2002; 15, 245-52.
6. Wang Y, Ma X, Zhou M, et al. Contribution of visceral fat accumulation to carotid intima-media thickness in a Chinese population. Int J Obes, 2012; 36, 1203-8.
7. Joint Committee for Developing Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults. Chinese guidelines on prevention and treatment of dyslipidemia in adults. Zhonghua Xin Xue Guan Bing Za Zhi, 2007; 35, 390-419. (In Chinese)
8. Ye Y, Bao Y, Hou X, et al. Identification of waist circumference cutoffs for abdominal obesity in the Chinese population: a 7.8-year follow-up study in the Shanghai urban arear. Int J Obes, 2009; 33, 1058-62.
9. Nambi V, Chambless L, Folsom AR, et al. Carotid intima-media thickness and the presence or absence of plaque improves prediction of coronary heart disease risk in the Atherosclerosis Risk in Communities (ARIC) study. J Am Coll Cardiol, 2010; 55, 1600-7.
10. Department of Noncommunicable Disease Surveillance 1999 Report of a WHO Consultation: definition, diagnosis and classification of diabetes mellitus and its complication. Part1: diagnosis and classification of diabetes mellitus. Geneva: World Health Organization.
11. Landsberg L, Aronne LJ, Beilin LJ, et al. Obesity-related hypertension: pathogenesis, cardiovascular risk, and treatment-a position paper of the Obesity Society and the American Society of Hypertension. Obesity, 2013; 21, 8-24.
12. Zhang ML, Hou XH, Zhu YX, et al. Metabolic disorders increase the risk to incident cardiovascular diseases in middle-aged and elderly Chinese. Biomed Environ Sci, 2012; 25, 38-45.
13. Alberti KG, Zimmet P, and Shaw J. Metabolic syndrome--a new world-wide definition. A consensus statement from the International Diabetes Federation. Diabet Med, 2006; 23, 469-80.
14. Bao Y, Lu J, Wang C, et al. Optimal waist circumference cutoffs for abdominal obesity in Chinese. Atherosclerosis, 2008; 201, 378-84.
15. Lakka TA, Lakka HM, Salonen R, et al. Abdominal obesity is associated with accelerated progression of carotid atherosclerosis in men. Atherosclerosis, 2001; 154, 497-504.
16. Shen Y, Zhang L, Zong WH, et al. Correlation between waist circumference and carotid intima-thickness in women from Shanghai, China. Biomed Environ Sci, 2013; 26, 531-8.
17. Alberti KG, Eckel RH, Grundy SM, et al. Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation, 2009; 120, 1640-5.
18. Khalil A, Huffman MD, Prabhakaran D, et al. Predictors of carotid intima–media thickness and carotid plaque in young Indian adults: The New Delhi Birth Cohort. Int J Cardiol, 2013; 167, 1322-8.
19. Han JH, Park HS, Kim SM, et al. Visceral adipose tissue as a predictor for metabolic risk factors in the Korean population. Diabet Med, 2008; 25, 106-10.
20. Seo JA, Kim BG, Cho H, et al. The cutoff values of visceral fat area and waist circumference for identifying subjects at risk for metabolic syndrome in elderly Korean: Ansan Geriatric (AGE) cohort study. BMC Public Health, 2009; 9, 443.
21. Nakamura K, Nanri H, Hara M, et al. Optimal cutoff values of waist circumference and the discriminatory performance of other anthropometric indices to detect the clustering of cardiovascular risk factors for metabolic syndrome in Japanese men and women. Environ Health and Prev Med, 2011; 16, 52-60.
22. Nikolopoulou A and Kadoqlou NP. Obesity and metabolic syndrome as related to cardiovascular disease. Expert Rev Cardiovasc Ther, 2012; 10, 933-9.
23. Yang Y, Hayden MR, Sowers S, et al. Retinal redox stress and remodeling in cardiometabolic syndrome and diabetes. Oxid Med Cell Longev, 2010; 3, 392-403.
24. Kawamoto R, Ohtsuka N, Ninomiya D, et al. Association of obesity and visceral fat distribution with intima media thickness of carotid arteries in middle-aged and older person. Intern Med, 2008; 47, 143-9.