Original Article

Visceral Fat Area, Waist Circumference and Metabolic Risk Factors in Abdominally Obese Chinese Adults*

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Abstract

Objective To examine the association of visceral adiposity as measured by VFA and WC with lipid and glucose metabolic biomarkers in abdominally obese Chinese adults, and to assess whether WC could be an indicator of visceral fat.

Methods WC and VFA were measured in 155 overweight and obese adults. A fasting blood sample was collected from participant (n=118) whose VFA $\geqslant$100 cm^2 for analyses of lipid and glucose profile. The relationship between VFA and WC and biomarkers was investigated.

Results WC and VFA were significantly interrelated. The coincidence rate of abdominal obesity determined by Japanese VFA and Chinese WC criteria increased across age quartiles in women from 51.7% to 96.2%. A large WC was associated significantly with low HDL-cholesterol concentration (P<0.01) and the association was weakened by additional control of VFA. WC and VFA were positively associated with glucose, hemoglobin A_{1c} and insulin concentrations (P<0.05 except for the association of VFA with insulin: P<0.01), and all the associations were not significant by additional control of either WC or VFA. As WC quartiles increased, significant stepwise increments in triglyceride, glucose, hemoglobin A_{1c} and insulin and descent in HDL-cholesterol were observed. However, triglyceride and HDL-cholesterol were not significantly different when compared across VFA quartiles.

Conclusion Higher visceral fat was associated with an adverse lipid and glucose profile. WC can be a moderate predictor for visceral fat and provides a feasible measurement to estimate glucose metabolic risks. Further studies are warranted to establish age-specific WC cutoffs.

Key words: Abdominal fat; Waist circumference; Lipid metabolism; Glucose metabolism

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INTRODUCTION

A wealth of studies have demonstrated a relationship between abdominal fat distribution and metabolic risk factors[1-3]. In particular, the accumulation of visceral adipose tissue has been shown to be a predictor for the onset of metabolic disorders and diseases including impaired glucose tolerance[4-5], insulin resistance[6], dyslipidemia[7-9], type 2 diabetes[10-11], hypertension[12-13], and metabolism syndrome[14], all of which are associated with an increased risk of developing cardiovascular diseases (CVD).

Nevertheless, available data evaluating the association of visceral adipose tissue with metabolic risk factors in Chinese adults are limited. Some studies have shown that compared with Westerners, Asian populations have more visceral adipose tissue and

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so take greater CVD risk at similar body mass index (BMI) and waist circumference (WC) levels[15-19]. This finding suggests that the visceral adipose tissue may be particularly sensitive to metabolic risks in Asians.

Computed tomography (CT) and magnetic resonance imaging (MRI) are precise and reliable imaging techniques for measuring regional adipose tissue distribution[20]. However, both methods require expensive equipment, and in the case of CT the subjects are potentially exposed to irradiation. Therefore, several anthropometric measurements, such as WC, waist-to-hip ratio (WHR), and abdominal sagittal diameter have been widely used to predict visceral adiposity and to detect the relationship between abdominal obesity and the metabolic profile[2,21-22]. It has been shown that among the simple anthropometric parameters, WC has the closest relationship with the measure of visceral adipose tissue[23-26]. It has not been verified whether this conclusion is applicable to the Chinese population, especially abdominally obese adults.

Thus, the aims of the present cross-sectional study are to assess whether visceral fat area (VFA) and WC are associated with lipid and glucose metabolism biomarkers and to investigate the feasibility of using WC as a predictor for visceral fat contents in abdominally obese Chinese adults.

MATERIALS AND METHODS

Study Sample

All the participants were aged 20-65 years with BMI$\geqslant$24. Criteria for exclusion included metabolic diseases that would require treatment (e.g., diabetes, hypertension, dyslipidemia, and coronary heart disease), a weight loss of $\geqslant$5% of the usual body weight in past three months, pregnancy or planning to become pregnant in the next three years, and current lactation. A total of 155 individuals were recruited after pre-screening from the local community of Beijing Municipality. These participants underwent abdominal adipose tissue measurements and physical examinations. Then, 118 participants were selected based on the criterion of VFA$\geqslant$100 cm^2 for further blood analyses. The study was approved by the institutional review boards of the Chinese Center for Disease Control and Prevention. All participants provided written informed consents.

Abdominal Adipose Tissue

Imaging of the abdomen was performed by using SOMATOM® Definition Computerized Tomography (Siemens, Munich, Germany). A cross-sectional scan of 10-mm thickness centered at the L4-L5 vertebral disc space was obtained with the participant in the supine position with both arms stretched above his/her head. The areas of visceral and subcutaneous adipose tissue (expressed in square centimeters) were calculated by using the software package "306_abdomen_FAT system" (306 Military Hospital of China, Beijing, China). Fat pixels were identified (image display window width -160 to -20 Hounsfield units [HU]) and the abdominal muscular wall was manually traced to separate the viscera from the subcutaneous compartment. The ratio between subcutaneous (S) and visceral (V) fat area (S:V ratio, SVR) was calculated as an indicator of the predominance of fat accumulation. VFA and SFA were summed to obtain the total abdominal fat area (TFA). Since there was no established criterion for abdominal obesity based on VFA in China, we adopted the Japanese criterion (VFA $\geqslant$100 cm^2) in the analyses[27].

Anthropometry

Weight (to the nearest 0.1 kg) and height (to the nearest 0.1 cm) were measured while the subjects were fasting and wearing light clothes without shoes. Weight was assessed with a balance-beam scale and height with a stadiometer. BMI was calculated as weight (in kilograms) divided by the square of height (in meters). WC and hip circumference (HC) were measured (to the nearest 0.1 cm) with a non-elastic tape while the participant was standing: WC was measured at the end of normal expiration and at the midpoint between the last rib and the crest of the ilium in a horizontal plane, and HC was recorded at the level of the symphysis pubic and the widest gluteal protuberance. WHR, defined as WC divided by HC, was then calculated to assess body fat distribution.

Metabolic Variables

Blood samples were collected in the morning after a 12-h fast to measure serum lipid and glucose metabolic biomarkers including total cholesterol (TCHO), triglyceride (TG), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), fasting blood glucose (FBG), hemoglobin A_{1c} (HbA_{1c}), and fasting insulin (FINS). The analyses were conducted by using AU2700® Chemistry-Immuno Analyzer (Olympus, Tokyo, Japan), HLC®-723G7 Automated Glycohemoglobin Analyzer (Tosoh, Tokyo, Japan), and IMMULITE® 1000 Immunoassay Analyzer

(Siemens, Munich, Germany).

Statistical Analysis

Differences between men and women were tested with the unpaired Student's *t*-test. An analysis of covariance was performed in order to compare the differences between men and women after the effects of age and BMI were removed. Pearson correlation coefficients were used to quantify the relationships between VFA, WC, and metabolic markers. Meanwhile, partial correlation coefficients were computed with age and BMI as covariates. Multivariable linear regression was used to assess the significance of age- and BMI-adjusted cross-sectional relation between WC, and VFA. R^2 values were computed to assess the relative contribution of WC to explanation of the variation in VFA.

In order to describe the redistribution of abdominal fat depot with age, participants were divided into age quartiles and least-squares means were calculated to assess the relative amounts of WC, VFA, and SVR by age quartiles after the effect of BMI was controlled. The trends in the coincidence rate of VFA and WC were analyzed by using Cochran-Armitage test. Similarly, participants were also divided into quartiles of VFA and WC, and least-squares means were calculated to assess the relative values of metabolic risk factors by quartiles of VFA and WC after age and BMI were controlled.

A value of $P<0.05$ was considered to be statistically significant. All analyses were performed by using the SAS statistical package (Version 9.13, SAS Institute, Cary, NC, USA).

RESULTS

Anthropometric and Metabolic Variables of Participants

Anthropometric and abdominal fat measurements for all participants and subgroups of men and women are shown in Table 1. On average, men were younger than women. There was no significant gender difference in BMI, and both mean BMIs exceeded 30.0 kg/m^2, the cutoff point for obesity defined by the World Health Organization (WHO). WC, WHR, and VFA were larger in men than in women. However, the total abdominal fat area (TFA) and the subcutaneous fat area (SFA) exhibited the reverse trend. Furthermore, the calculated SVR was significantly higher in women than in men. The coincidence rates of abdominal obesity decided by using the Japanese VFA criterion and Chinese WC cutoff points (WC $\geqslant$85 cm in men and $\geqslant$80 cm in women) were 96% for men and 80% for women.

Table 1. Anthropometric Characteristics and Abdominal Fat Levels of All Simple Overweight and Obese Participants ($\bar{x}\pm s$)

	All (*n*=155)	Men (*n*=50)	Women (*n*=105)
Age (years)	44.1±10.0	38.8±8.8	46.7±9.5***
BMI (kg/m^2)	30.5±3.1	30.9±3.7	30.4±2.8
WC (cm)	98.2±9.0	104.0±9.3	95.5±7.5***
WHR (cm/cm)	0.9±0.1	1.0±0.1	0.9±0.1***
TFA (cm^2)	496.2±104.4	470.2±113.1	508.5±98.1*
SFA (cm^2)	348.0±91.1	306.5±98.3	367.8±80.8**
VFA (cm^2)	148.2±46.3	163.7±46.8	140.8±44.5**
SVR (cm^2/ cm^2)	2.6±1.1	2.0±0.8	2.9±1.1***
Coincidence Rate† (%)	85.2	96.0	80.0

Note. Abbreviations: BMI=body mass index; WC=waist circumference; WHR=waist-hip ratio; TFA=total abdominal fat area; SFA=subcutaneous fat area; VFA=visceral fat area; SVR=SFA-VFA ratio. †Conformity of diagnoses of abdominal obesity using Japanese visceral fat area and Chinese waist circumference criteria. $^{*}P<0.05$, $^{**}P<0.01$, $^{***}P<0.001$, significantly different from males.

Table 2 shows the anthropometric and metabolic marker measurements among those with a VFA $\geqslant$100 cm^2. WC, WHR, and VFA were greater still in men than in women. Lipid and glucose metabolism biomarkers were somewhat similar between men and women, only the results for HDL were significantly higher in women than in men. According to the cutoff points provided by the laboratory, means of TG, HDL, and HbA_{1c} deviated from the normal ranges.

Correlations Between Waist Circumference and Visceral Fat Area

Further analyses illustrated that WC and VFA increased but SVR decreased with age in women (Table 3). The coincidence rate of Japanese VFA and Chinese WC criteria also increased across age quartiles in women. On the other hand, WC, VFA, SVR, and the coincidence rate did not show a change with age in men. In addition, WC and VFA were strongly and significantly interrelated (Table 4). This was true among the 155 participants or the 118 participants with a VFA $\geqslant$100 cm^2, and in gender subgroups (all $P<0.001$ except for men: $P<0.05$). Meanwhile, results from multivariable linear regression showed that WC was associated with nearly 30% of the variation

in VFA after adjustment for age and BMI in the 155 participants or the 118 participants with a VFA $\geqslant$100 cm^2 (partial R^2=0.3144 and 0.2865, respectively).

Table 2. Characteristics of Abdominally Obese Participants Who Had Blood Tests after Being Adjusted for Age and BMI ($\bar{x}\pm SE$)

	Men (*n*=44)	Women (*n*=74)
WC (cm)	104.4±0.9	96.6±0.7**
WHR (cm/cm)	1.0±0.01	0.9±0.01**
TFA (cm^2)	486.4±9.3	519.8±6.6*
SFA (cm^2)	302.7±9.1	368.7±6.4**
VFA (cm^2)	183.8±5.7	151.1±4.0**
SVR (cm^2/cm^2)	1.7±0.1	2.5±0.1**
TCHO (mmol/L)	5.39±0.13	5.32±0.09
TG (mmol/L)	2.72±0.30	2.03±0.21
HDL (mmol/L)	1.03±0.04	1.21±0.03**
LDL (mmol/L)	3.23±0.12	3.17±0.09
FBG (mmol/L)	5.5±0.1	5.2±0.1
HbA_{1c} (%)	6.0±0.1	5.8±0.1
FINS (miu/L)	11.54±0.92	10.31±0.65

Note. Abbreviations: BMI=body mass index; WC=waist circumference; WHR=waist-hip ratio; TFA=total abdominal fat area; SFA=subcutaneous fat area; VFA=visceral fat area; SVR=SFA-VFA ratio; TCHO=total cholesterol; TG=triglycerides; HDL=high-density lipoprotein cholesterol; LDL=low-density lipoprotein cholesterol; FBG=fasting blood glucose; HbA_{1c}=hemoglobin A1c; FINS=fasting insulin. *P<0.05, **P<0.001, significantly different from males.

Table 4. Correlation Coefficients between VFA and WC in All Simple Overweight and Obese and Abdominally Obese Participants Who Had Blood Tests

		Unadjusted	Age-and BMI-Adjusted
Overweight and Obesity	All (*n*=155)	0.56**	0.56**
	Men (*n*=50)	0.45**	0.33*
	Women (*n*=105)	0.57**	0.50**
Abdominal Obesity	All (*n*=118)	0.54**	0.51**
	Men (*n*=44)	0.46*	0.31*
	Women (*n*=74)	0.58**	0.47**

Note. *P<0.05, **P<0.001.

Association of Visceral Adipose Tissue with Lipid and Glucose Metabolic Variables

Figure 1 illustrates the magnitudes of the correlation coefficients between VFA and WC with the metabolic variables (TCHO, TG, HDL, LDL, FBG, HbA_{1c}, FINS), respectively, in the 118 participants. With the simple correlation analysis, VFA was significantly correlated with TCHO, HbA_{1c}, and FINS. WC was significantly correlated with TG, HDL, and FINS. However, after being adjusted for age and BMI, VFA was significantly correlated with FBG, HbA_{1c}, and FINS, whereas WC was correlated with HDL, FBG, HbA_{1c}, and FINS. After further adjustment for either WC or VFA, none of the associations remained. The only exception was that VFA was correlated with FINS independent of age and BMI in women both before (r=0.38, P<0.01) and after control of WC (r=0.34, P<0.01), whereas a significant correlation was found between WC and FBG independent of age and BMI in men before control of VFA (r=0.33, P<0.05).

Table 3. Distribution of Abdominal Fat Depots and Coincidence Rate of WC and VFA across Age Quartiles in All Simple Overweight and Obese Participants after Being Adjusted for BMI ($\bar{x}\pm SE$)

Age Quartile	Men (*n*=50)				Women (*n*=105)			
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Quartile 1	Quartile 2	Quartile 3	Quartile 4
WC (cm)	104.3±1.4	103.4±1.7	103.8±1.5	104.4±1.6	94.4±1.1	93.7±1.2	96.2±1.1	97.6±1.1*
VFA (cm^2)	144.2±11.0	182.4±13.6	158.7±11.9	181.1±13.0	111.2±6.4	124.9±7.0	154.6±6.8	174.5±6.7*
SFA (cm^2)	323.2±14.1	277.1±17.4	318.8±15.2	294.6±16.6	365.6±10.5	368.2±11.6	363.6±11.2	374.0±11.1
SVR (cm^2/ cm^2)	2.3±0.2	1.6±0.2	2.2±0.2	1.7±0.2	3.5±0.2	3.2±0.2	2.4±0.2	2.3±0.2*
Coincidence Rate† (%)	93.8	100.0	92.3	100.0	51.7	75.0	100.0	96.2*

Note. Abbreviations: WC=waist circumference; VFA=visceral fat area; SFA=subcutaneous fat area; SVR=SFA-VFA ratio. †Conformity of diagnoses of abdominal obesity using Japanese visceral fat area and Chinese waist circumference criteria. *P<0.05 for the trend across age quartiles in the men or women group.

In order to identify which metabolism biomarkers varied in close association with VFA and WC, we subdivided the 118 participants into quartiles of VFA and WC, and examined the trends in these metabolism biomarkers across VFA and WC quartiles, independent of age and BMI. As shown in Figure 2, a significant increment of TG and a significant descent of HDL were observed across WC quartiles, and FBG, HbA_{1c}, and FINS increased significantly across both VFA and WC quartiles. To verify the potential gender difference in the relationships between visceral adipose tissue and metabolism biomarkers, we examined the above associations by gender also. In men, only FINS increased progressively across quartiles of VFA and WC. In women, rising trends were found in HbA_{1c} and FINS across levels of VFA, and in TG and FINS across levels of WC. Decreasing of HDL was evident as WC increased in women. However, these trends in gender subgroups were not significant except FINS across VFA quartiles in women (P=0.0008).

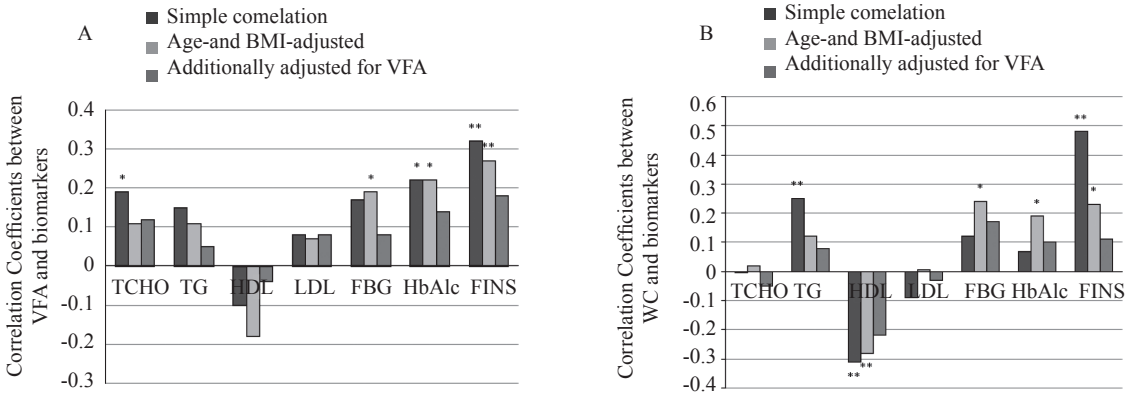

Figure 1. Correlation coefficients between visceral fat area (A) and waist circumference (B) and metabolic variables (n=118). Abbreviations: BMI=body mass index; VFA=visceral fat area; WC=waist circumference; TCHO=total cholesterol; TG=triglycerides; HDL=high-density lipoprotein cholesterol; LDL=low-density lipoprotein cholesterol; FBG=fasting blood glucose; HbA_{1c} =hemoglobin A_{1c}; FINS=fasting insulin. $^{*}P$<0.05, $^{**}P$<0.01.

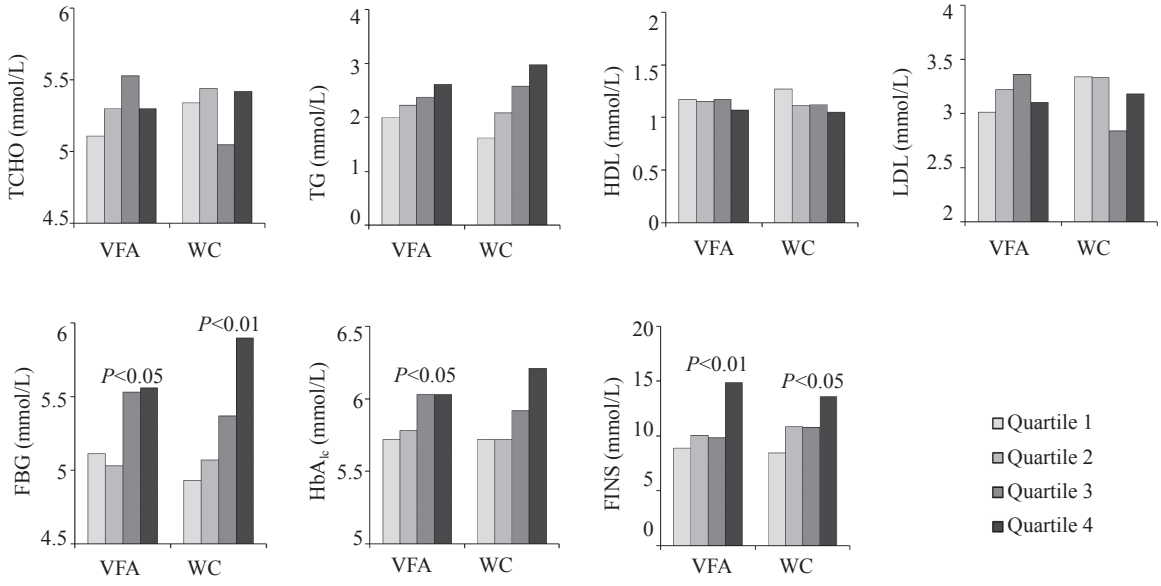

Figure 2. Variations in lipid and glucose metabolism biomarkers concentrations according to quartiles of visceral fat area and waist circumference after adjustment for age and BMI (n=118). Abbreviations: BMI=body mass index; VFA=visceral fat area; WC=waist circumference; TCHO=total cholesterol; TG=triglycerides; HDL=high-density lipoprotein cholesterol; LDL=low-density lipoprotein cholesterol; FBG=fasting blood glucose; HbA_{1c}=hemoglobin A_{1c}; FINS=fasting insulin. P<0.05 or P<0.01 for the trend across VFA or WC quartiles.

DISCUSSION

Previous studies have revealed that visceral adipose tissue has high activities of both lipogenesis and lipolysis, and its accumulation induces a high content of free fatty acids in portal circulation which goes into the liver directly[28-29]. Excess free fatty acid may cause the enhancement of lipid synthesis and gluconeogenesis as well as insulin resistance, resulting in hyperlipidemia, glucose intolerance, hypertension, and atherosclerosis[29-31]. Thus, excess visceral adipose tissue is believed to be an important contributor to the development of CVD. In the present study, VFA and WC were observed to be closely associated with glucose metabolic risk factors including FBG, HbA_{1c}, and FINS in abdominally obese Chinese adults after control of age and BMI. This finding confirms that visceral adipose tissue is associated with glucose metabolism. In fact, a similar finding was observed in other populations. Hayashi and his coworkers have proposed that a greater visceral adiposity increases the risk of impaired glucose tolerance[5], which is consistent with Goodpaster's findings[4]. High FBG, HbA_{1c}, and FINS values indicate a relatively high risk for the future development of diabetes as well as CVD. The association between visceral adipose tissue and lipid metabolism biomarkers is not so evident in our study. After adjustment for age and BMI, only HDL was significantly correlated with WC. In Figure 2, a downward trend in HDL and a rising trend in TG were observed as the visceral adipose tissue increased, which was in agreement with Onat and Pouliot's reports[25-26]. A high TG level has been shown to be a risk factor for CVD independent of HDL[32]. HDL is inversely correlated with the risk of CVD and a low HDL level is one of the hallmarks of the metabolic syndrome[33-34]. Although TCHO and LDL did not show linear trends as expected, we cannot deny the existence of their relationship with visceral adiposity. These results should be interpreted with caution because of the relatively small number of participants studied and the narrow range of individual variation of visceral adiposity in the present study.

In the present study, WC was closely correlated with the amount of abdominal visceral fat. However, the results for diagnosis of abdominal obesity with VFA and WC criteria were not the same, especially in women. This may be partly due to the Japanese criterion we used, which may not be applicable to abdominally obese Chinese adults. In addition, the VFA criterion is the same for men and women whereas the WC criterion is different. It would be worthwhile to further explore whether VFA $\geqslant$100 cm^2 indicates metabolic risks to the same extent in both genders. Another concern was that men were significantly younger and had a narrower age range than women in the present study. Lemieux and his colleagues suggested that age should be taken into account in the estimation of VFA from WC. For corresponding amounts of visceral adipose tissue, threshold values of WC were generally lower among subjects aged >40 years than among those who were $\leqslant$40 years in both men and women[35], which is in agreement with Kuk's results[36]. In fact, the age-related redistribution of abdominal fat depends on an absolute and relative increment of visceral fat depots as shown in Table 3. As an indicator of the total amount of abdominal adiposity, WC does not distinguish visceral adiposity from the amount of subcutaneous abdominal fat, and thus, it cannot reflect fat redistribution and the coincidence rate of WC with VFA changes with the increase of age. In the women participants of this study, the coincidence rate was markedly lower in younger age groups than in older age groups. Thus, the current WC criterion will require an age-specific adjustment according to abdominal fat redistribution in the future. Although the WC criterion equivalent to the criterion of VFA $\geqslant$100 cm^2 remains unclear, our analyses reveal that WC can be used as an approximate index of abdominal visceral adiposity and in the assessment of metabolic risks. The association of WC with metabolic biomarkers demonstrated similar trends as VFA, independent of age and BMI, which suggests that WC contributes important information on visceral adiposity. Moreover, the associations of VFA with glucose metabolic risk factors (FBG, HbA_{1c}, and FINS) were weakened by additional control of WC. Correspondingly, additional adjustment for VFA weakened the relationship between WC and metabolism biomarkers (HDL, FBG, HbA_{1c}, and FINS). This finding illustrates that VFA can account for the relationship between WC and metabolic risk factors, and WC can partly substitute for VFA in describing the effect of visceral adiposity on metabolic profile, especially glucose metabolism.

Gender differences in abdominal fat distribution were observed in this abdominally obese population. Table 1 shows that even at a younger age, men had greater visceral adipose tissue than women at the same BMI, which means that men tend to accumulate more fat within the abdominal cavity[37-38]. From clinical and basic experiments, a number of factors have been suggested to be strongly associated with

visceral fat accumulation, including aging, imbalance of sex hormones, cigarette smoking, lack of physical activity, and low dietary fiber intake[29-30,39]. Among these factors, hormones play a major role that contributes to gender differences. In addition, some genetic variables may act in a sex-specific manner: for example, genetic polymorphisms can affect lipogenesis and lipolysis differently in men and women[40]. These sex differences in fat metabolism may partly explain the well-documented sex differences associated with the incidence of CVD risk factors, which are supported by Fox and Lemieux, as well as the findings of the present study[37,41]. After adjustment for age and BMI, men tended to have more unfavorable lipid and glucose metabolism biomarkers compared with women. In the analyses of the association between visceral adipose tissue and metabolic risk factors, WC was significantly associated with only FBG in men while VFA was significantly associated with only FINS in women. In addition, only FINS increased significantly across quartiles of VFA in women. The discrepancy in the findings may in part be attributable to the gender-specific differences. However, since the present study was performed in abdominally obese adults with a small sample size, the narrower ranges of BMI, abdominal fat amount and blood biomarkers may weaken gender differences.

Limitations include the cross-sectional design, which does not allow us to make causal inferences. In addition, our results cannot be extrapolated to the general population in China because of non-random sampling of abdominally obese subjects. Another concern is the difference in age range between genders. Despite adjustment for age in the statistical analyses, the data for middle-aged and older men were limited. Finally, diet, physical activity, cigarette smoking, alcohol intake, and other data were not recorded to assess the contribution of these factors to the metabolic abnormality.

In conclusion, our study indicates that among these abdominally obese Chinese adults, an increasing level of visceral adiposity is associated with a significant increase of lipid and glucose metabolism values. In addition, our results suggest that WC can be an approximate indicator of abdominal obesity and provides a feasible measurement to estimate glucose metabolic risks in large scale studies. Further studies are warranted to establish age-specific WC cutoffs.

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