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ORIGINAL ARTICLE

Influence of central obesity on clustering of metabolic syndrome risk variables among normal-weight adults in a low-income rural Chinese population

Shiying Fu · Zelin Xiang · Yujuan Zhao · Lili Ling · Congju Wang · Jialiang Xu · Jingbo Zhao

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Abstract
Aim This study aimed to examine the influence of central obesity on the clustering patterns of adverse levels of metabolic syndrome (MetS) risk variables among adults with normal weight in a low-income rural Chinese cohort.
Subject and methods The study cohort consisted of 1,821 adults, aged 35–74 years. Central obesity was defined as a waist to height ratio≥0.5 among adults with normal weight (body mass index=18.5–24.9). MetS risk variables included blood pressure (BP), fasting triglycerides and glucose, and high-density lipoprotein cholesterol (HDL-C).
Results Centrally obese subjects had significantly higher levels of all the MetS risk variables than those without central obesity. The central obesity group had a higher prevalence of MetS (clustering of three or more variables) than the control group (13.9 vs 5.8%, $p<0.001$). Importantly, the cluster of high triglycerides, low HDL-C, and high BP showed the greatest difference ($p<0.001$) between the two groups. In multivariable logistic regression analyses, adjusting for age, sex, smoking, and alcohol drinking, the centrally obese group vs the control group was 2.25 times more likely to have MetS ($p<0.01$). Among the four types of three variable clusterings, central obesity was significantly associated with the cluster of high triglycerides, low HDL-C, and high BP (odds ratio=3.51, $p<0.01$).
Conclusion These findings indicate that the central obesity detected by the waist to height ratio plays a pivotal role in the clustering of MetS risk variables among normal-weight Chinese adults, suggesting the importance of prevention of MetS by reducing central obesity in a population with a lower prevalence of obesity.

Keywords Central obesity · Normal weight · Waist to height ratio · Metabolic syndrome · Chinese population

S. Fu · Y. Zhao
Department of Cardiology, The First Affiliated Hospital,
Harbin Medical University,
Harbin, China

Z. Xiang · L. Ling · C. Wang · J. Xu · J. Zhao (✉)
Department of Epidemiology, School of Public Health,
Harbin Medical University,
157 Baojian Road,
Nangang District, Harbin 150086, China
e-mail: Zhaojb168@sina.com

Introduction

Metabolic syndrome (MetS), the concurrence of inextricably linked disorders, including obesity, insulin resistance, dyslipidemia, and hypertension (Reaven 1997; DeFronzo and Ferrannini 1991), has gained importance because of its association with subsequent morbidity and mortality from cardiovascular (CV) disease (Lakka et al. 2002). The National Cholesterol Education Program (NCEP) in its most recent Adult Treatment Panel III (ATP III) report recognized MetS as a highly important CV risk entity (Expert Panel on Detection, Evaluation, and Treatment 2001). According to the NCEP ATP III definition, about 47 million US residents have MetS (Ford et al. 2002). Although the pathophysiologic mechanisms underlying the development of MetS are not fully understood, obesity is generally considered a determinant of clustering of the MetS components (Srinivasan et al. 2002; Chen et al. 2000). Interestingly, not all obese individuals display clustering of the MetS variables. On the other hand, there is a subgroup of individuals who have normal weight and body mass index (BMI), but display a cluster of obesity-related metabolic abnormalities. This group of individuals has been reported and described in detail since the 1980s (Ruderman et al. 1982, 1998; Karelis et al. 2004). Recently, central obesity among individuals with normal weight has received increasing attention with respect to its role in the development of MetS (Hsieh and Muto 2005; Conus et al. 2004; Srinivasan et al. 2009; Hsieh and Yoshinaga 1995a, b).

Asian populations have a relatively lower BMI (Molarius et al. 1999; WHO Expert Consultation 2004), but are predisposed to visceral or abdominal obesity. At the same BMI level, body fat percentage is higher in Asians than in Caucasians (Fujimoto et al. 1995; Chang et al. 2003; Deurenberg et al. 1998, 2002; Gurrici et al. 1998; Wen et al. 2009). Further, central fat accumulation is reported to be more strongly associated with MetS variables than peripheral fat distribution (Hsieh and Yoshinaga 1995a, b; Deurenberg-Yap et al. 2002; Wildman et al. 2005). The rapid economic development has been accompanied by westernization of lifestyle behaviors and an increasing epidemic of obesity in China during the past couple of decades (Cheng 2004; Reynolds et al. 2007). However, information is limited regarding the role of central obesity measured by a waist to height (W/H) ratio in the clustering of adverse MetS variables among normal-weight Chinese adults. The present study examined this aspect in a cohort of adults living in a low-income rural area in northeast China, a population with a low prevalence of obesity.

Methods

Study subjects

Lanxi County located in northeast China has been categorized as a nationwide low-income county based on the regional economic levels and residents' income since 1978. A cross-sectional survey was conducted in 2007. Eleven villages in Pingshan Town of Lanxi County were randomly selected as study fields using a cluster sampling procedure. A total of 3,012 adults, aged 35–74 years, were examined for CV disease risk factors, with a participation rate of 86.6%. Details of the protocol have been described elsewhere (Wang et al. 2008). After data editing and cleaning, 2,967 participants (1,324 men and 1,643 women) were eligible for analysis. Of these, 1,821 subjects (844 men and 977 women) whose BMI was between 18.5 and 24.9 were considered normal weight and retained for this analysis.

All subjects in this study gave informed consent. Study protocols were approved by the Ethics Committee of Harbin Medical University.

Measurements

Anthropometric measurements Height and weight were measured to±0.1 cm and to ± 0.1 kg, respectively. BMI (weight in kilograms divided by the square of the height in meters) was used as a measure of overall adiposity. Waist circumference was measured midway between the lower border of the rib cage and the superior border of the iliac crest while the subject was standing. Replicate measurements were made and mean values were used for analysis. Based on the previously recommended cutoff point (Srinivasan et al. 2009; Hsieh and Yoshinaga 1995a, b), study subjects with a W/H ratio≥0.5 were grouped as centrally obese normal weight (n=560) and the rest was used as a control group (n=1,261). In this study, we used the term "central obesity" for convenience to describe the "centrally obese normal weight" condition.

Blood pressure (BP) BP levels were measured at 8:00 to 10:00 in the morning. After resting for 10 min, indirect BP was recorded on the right arm of subjects in a sitting position by a trained observer (two replicates) using a mercury sphygmomanometer. Systolic and diastolic BP were recorded at the first and fifth Korotkoff phases, respectively. Hypertension was defined as systolic BP≥ 140 mmHg or diastolic BP≥90 mmHg or under antihypertensive treatment. In the analysis of MetS, high levels of BP were defined by ATP III guidelines (systolic BP≥ 130 mmHg or diastolic BP≥85 mmHg or under antihypertensive treatment).

Questionnaire Information on demographics, tobacco use, alcohol consumption, personal health, and medication history was obtained by questionnaires. Current smoking was defined as smoking at least one cigarette a day during the past 6 months; current drinking was defined as drinking beer, wine, or spirits at least once a week during the past 6 months.

Laboratory measurement Participants were instructed to fast for 12 h before screening, and compliance with fasting was determined by interview on the morning of the examination. Antecubital venous blood was collected for serum and plasma. Serum triglycerides and high-density lipoprotein cholesterol (HDL-C) were analyzed by enzymatic procedures; plasma glucose was measured by an enzymatic method using commercial kits (Lanyi Science and Technology Co. Ltd., Shanghai, China) on the multichannel Olympus AU5400 Autoanalyzer (Tokyo, Japan) in the laboratory of the First Affiliated Hospital of Harbin Medical University.

Statistical methods

All data analyses were performed using SAS version 9.1. Differences in mean values of the MetS variables between the central obesity and control groups were tested by analysis of covariance in a generalized linear model (GLM), adjusting for age and sex. Differences in percentages of categorical variables were tested by a chi-square test. Triglyceride values were log-transformed to improve normality of the distribution prior to analysis of covariance; however, the mean values in the original scales are presented in Table 1 for description. Adverse levels of the MetS variables (high BP, high triglycerides, low HDL-C, and high glucose) were defined by ATP III guidelines (Expert Panel on Detection, Evaluation, and Treatment 2001). For trend analysis of the W/H ratio by number of MetS risk variables, covariate-adjusted means of the W/H ratio derived from the GLM were used. The independent associations between central obesity and clustering of three or four variables were examined by a multivariable logistic regression analysis model, using clustering (yes/no) as a dependent variable and central obesity (yes/no) as a independent variable, adjusting for age, sex, smoking, and drinking.

Results

Table 1 lists demographic and MetS variables in normal-weight (BMI=18.5–24.9) Chinese adults by central obesity status defined by the W/H ratio. Among normal-weight adults, subjects in the central obesity group (W/H≥0.5, n=560) constituted 30.8% of the study cohort (n=1,821). The central obesity group versus the control group was 4.6 years older. The central obesity group had more women than the group without central obesity. As one would expect, significant differences in the W/H ratio, waist circumference, and BMI between the two groups were noted because the two groups were defined by the W/H ratio and waist circumference. Importantly, the central obesity group had significantly higher levels of BP, triglycerides, and glucose and lower levels of HDL-C than the control group after adjusting for age and sex. The prevalence of smoking and drinking did not differ significantly between the two groups. It should be noted that the values of BP and glucose of subjects under treatment were deleted in Table 1. Hypertension prevalence was significantly higher in the central obesity group than in the control group.

Table 1 Characteristics of study subjects with normal weight (BMI=18.5–24.9) by waist circumference to height ratio

n	W/H<0.5 1,261	W/H≥0.5 560	*p* values[a]
Age (years)	51.1±11.0	55.7±11.3	<0.001
Males/females	615/646	228/332	0.002
Waist circumference (cm)	73.6±5.5	83.6±5.9	<0.001
W/H	0.46±0.03	0.53±0.03	<0.001
BMI (kg/m^2)	22.0±1.6	23.0±1.5	<0.001
Systolic BP (mmHg)[b]	126.3±20.7	133.3±23.4	<0.001
Diastolic BP (mmHg)[b]	80.0±11.7	82.5±13.2	0.001
Hypertension (%)[c]	32.4	45.9	<0.001
Triglycerides (mmol/l)	1.28±0.8	1.64±1.0	<0.001
HDL-C (mmol/l)	1.70±0.8	1.56±0.8	<0.001
Glucose (mmol/l)[d]	4.60±1.6	4.91±1.9	0.004
Smokers (%)	48.6	44.8	0.135
Drinkers (%)	26.6	26.8	0.922

W/H waist circumference to height ratio, *BMI* body mass index, *BP* blood pressure, *HDL-C* high-density lipoprotein cholesterol

[a] *p* values for comparison between the two groups adjusting for age and sex

[b] Values of BP of subjects under treatment (n=57 in the W/H<0.5 group and n=38 in the W/H≥0.5 group) were excluded

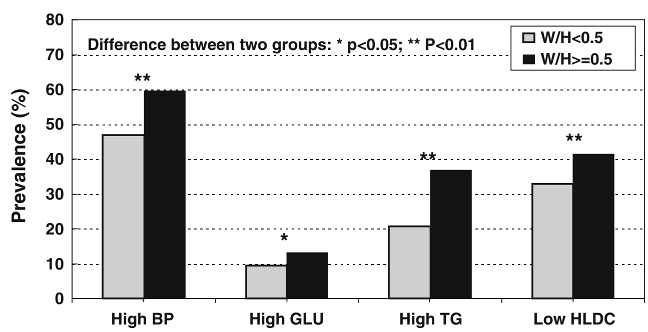
[c] Hypertension was defined by systolic BP≥140 or diastolic BP≥90 mmHg or under treatment

[d] Values of glucose of subjects under treatment (n=5 in the W/H<0.5 group and n=3 in the W/H≥0.5 group) were excluded

Figure 1 illustrates the prevalence of adverse levels of the MetS variables defined by ATP III guidelines among normal-weight Chinese adults by the W/H ratio. The prevalence rates of high BP, high glucose, high triglycerides, and low HDL-C in the central obesity group were all significantly greater than those in the control group. It should be pointed out that the prevalence rates of high BP were higher than those of hypertension in Table 1 because the high BP in Fig. 1 was defined as systolic BP≥130 mmHg and/or diastolic BP≥80 and/or under treatment.

Figure 2 shows the relationship between the W/H ratio and the number of MetS variables. Individuals who had more MetS variables showed significantly higher mean values of covariate-adjusted W/H ratio (p for trend <0.001). The covariates included age, sex, alcohol drinking, and smoking.

Figure 3 presents the three-risk variable clustering patterns among normal-weight Chinese adults by the W/H ratio. Among the four types of combinations, only



Adverse levels of MetS variables were defined by ATPIII guidelines. BP=blood pressure; TG= triglycerides; GLU= glucose; HDLC=high density lipoprotein cholesterol;

Fig. 1 Prevalence of adverse levels of MetS variables defined by ATP III guidelines among normal-weight (BMI=18.5–24.9) Chinese adults by waist circumference to height ratio (W/H)

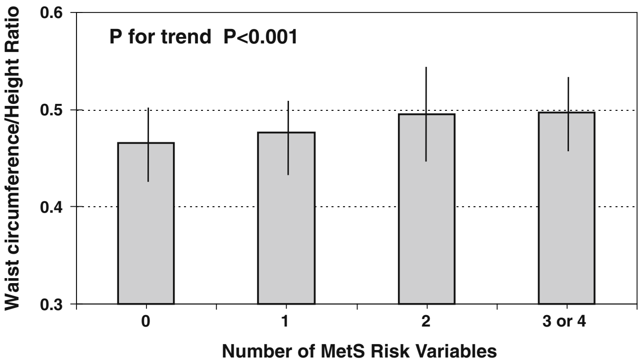


Fig. 2 Mean levels of covariate-adjusted waist circumference to height ratio by number of MetS variables defined by ATP III guidelines among normal-weight (BMI=18.5–24.9) Chinese adults

clustering of high triglycerides, low HDL-C, and high BP showed a significantly higher prevalence in the central obesity group than in the control group ($p<0.001$), which was largely because of the higher correlation between triglycerides and HDL-C in the central obesity group. The clustering of four variables did not significantly differ between the two groups ($p=0.126$). However, the central obesity group had a significantly higher prevalence of MetS (clustering of three or more variables) than the control group (13.9 vs 5.8%, $p<0.001$). The results shown in Fig. 3 were derived from univariate analyses without adjustment for any covariates.

Risk for MetS (clustering of three or four variables) and specific combinations of three variables in the central obesity group versus the control group derived from multivariable analyses is presented in Table 2. The central obesity group versus the control group was 2.25 times more likely to have MetS. Further, age, female sex, and smoking were also significantly associated with higher risk of MetS. Among the four combinations of three variables, central obesity was significantly associated with the clustering of high triglycerides, low HDL-C, and high BP, but not with other combinations of three variables. Of note, age was associated with clustering of three or four variables [odds ratio (OR)=1.03] and the cluster of high triglycerides, low HDL-C, and high BP (OR=1.02). The ORs were significant with small values because 1 year was used as the unit of age in the logistic regression model. OR=1.02 means that when age increases by 1 year, the risk for having the cluster increases 1.02 times. Accordingly, an increase of 10 years for age is associated with a risk of 1.22 times (1.02^{10}) for having the cluster of these three variables, i.e., an increase of 22% of the risk.

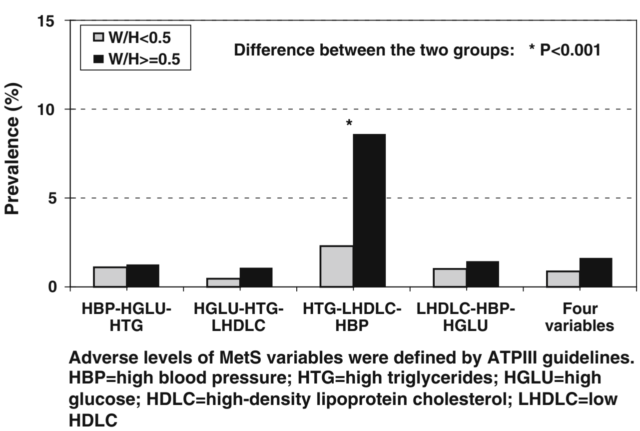


Fig. 3 Clustering of MetS variables among normal-weight (BMI=18.5–24.9) Chinese adults by waist circumference to height ratio (W/H)

Discussion

The current study used the W/H ratio to define central (visceral) obesity among normal-weight individuals in a low-income rural Chinese adult population and demonstrated that normal-weight subjects with central obesity versus those without central obesity had adverse levels of MetS components, including BP, triglycerides, HDL-C, and glucose. Importantly, the normal-weight adults with central obesity, compared with those without central obesity, are more likely to have clustering of multiple MetS components, especially the clustering of high BP, high triglycerides, and low HDL-C. These observations in a Chinese population are in accordance with the reports on subgroups of obesity and their phenotypic characteristics in terms of the constellation of MetS variables from previous studies in Asians (Hsieh and Muto 2005; Hsieh and Yoshinaga 1995a, b; Deurenberg-Yap et al. 2002) and other populations (Ruderman et al. 1982, 1998; Karelis et al. 2004; Conus et al. 2004; Srinivasan et al. 2009). The findings from the present study underscore the importance of the utility of the W/H ratio as a measure of abdominal fat accumulation in predicting MetS even among individuals with a normal weight in terms of BMI.

BMI and waist circumference have been widely used to define overweight and obesity (Expert Panel on Detection, Evaluation, and Treatment 2001; WHO Expert Consultation 2004). BMI is an indicator of overall obesity, but does not take into account the distribution of body fat. Asian populations have a higher risk of body fat accumulation at lower levels of BMI than do Western populations (Deurenberg et al. 1998, 2002; Gurrici et al. 1998; Wen et al. 2009). Although waist circumference has been advocated as an indicator of abdominal fat content, the cut points vary by race, sex, and country (Expert Panel on Detection, Evaluation, and Treatment 2001; Deurenberg-Yap et al. 2002; Wildman et al. 2005; Misra et al. 2005). Several studies have demonstrated the utility of the W/H ratio in detecting central obesity and related CV risk among normal-weight individuals

Table 2 Odds ratio (95% confidence interval) for MetS variable clustering associated with central obesity among normal-weight Chinese adults (BMI=18.5–24.9)

	Dependent variables				
	Three or four variables cluster	HBP-HGLU-HTG cluster	HGLU-HTG-LHDL-C cluster	HTG-LHDL-C-HBP cluster	LHDL-C-HBP-HGLU cluster
Age	1.03** (1.01–1.05)	1.03 (0.99–1.08)	0.99 (0.94–1.05)	1.02* (1.00–1.05)	1.03 (0.99–1.07)
Female	1.99** (1.26–3.16)	1.59 (0.49–5.16)	2.25 (0.44–11.5)	1.95* (1.04–3.67)	1.59(0.55–4.64)
Smoking	1.46* (1.03–2.09)	3.07* (1.08–8.76)	1.89 (0.56–6.35)	1.25 (0.77–2.04)	3.39* (1.28–8.97)
Drinking	1.28 (0.77–2.14)	2.34 (0.72–7.61)	1.30 (0.22–7.82)	0.99 (0.47–2.05)	0.59 (0.16–2.17)
W/H ratio	2.25** (1.59–3.19)	1.06 (0.41–2.70)	2.54 (0.79–8.20)	3.51** (2.15–5.71)	1.35 (0.54–3.37)

Adverse levels of MetS variables were defined by ATP III guidelines

Coding: dependent variables, 1 = cluster, 0 = no cluster; age in years; female = 1, male = 0; smoking, 1 = yes, 0 = no; drinking, 1 = yes, 0 = no; W/H ratio, 1 = central obesity, 0 = no central obesity

HBP high blood pressure, *HTG* high triglycerides, *HGLU* high glucose, *HDL-C* high-density lipoprotein cholesterol, *LHDL-C* low HDL-C, *W/H* waist to height ratio

*$p<0.05$; **$p<0.01$

(Hsieh and Muto 2005; Srinivasan et al. 2009; Hsieh and Yoshinaga 1995a, b, 2003). The prevalence of central obesity measured as W/H ratio≥0.5 among normal-weight individuals was 40.8% (45.5% in men and 28.3% in women) in a Japanese population and 10.2% among US adults (Flegal et al. 2002). In the current study 30.8% (27.1% in men and 33.9% in women) of Chinese adults with normal weight had central obesity. These observations provide further evidence that Asian people are more susceptible to abdominal or visceral deposition than Caucasians. Although the body fat distribution in relation to BMI levels has been extensively studied in Asian populations (Fujimoto et al. 1995; Chang et al. 2003; Deurenberg et al. 1998, 2002; Gurrici et al. 1998; Deurenberg-Yap et al. 2002; Low et al. 2009; Hsieh et al. 2003), data on central obesity measured as the W/H ratio are not available for comparison in a Chinese population. Further studies are needed to replicate the findings in this regard.

It is well known that abdominal fat accumulation is more strongly associated with increased CV risk and the development of MetS than peripheral fat distribution in various ethnic groups (Ruderman et al. 1982; Hsieh and Yoshinaga 1995a; Deurenberg-Yap et al. 2002; Wildman et al. 2005; Hsieh et al. 2003). Ruderman et al. introduced the concept of the “metabolically obese, normal-weight individuals.” This condition was defined as those who are not obese on the basis of height and weight, but hyperinsulinemic, insulin resistant, hypertriglyceridemic, and predisposed to type 2 diabetes with premature coronary heart disease (Ruderman et al. 1982, 1998). Attempts have been made to explore whether central obesity adds an independent CV risk to the assessment gained through measurement of BMI (Wildman et al. 2005; Ko et al. 1997; Seidell et al. 1990, 1992). Several reports from Asia suggested that the W/H ratio correlates with metabolic risk better than BMI, waist circumference, waist to hip ratio, and skinfold measures. The cutoff value for the W/H ratio (0.5) appears to be a simple but effective index for identifying central obesity for both overweight and normal-weight individuals with high CV risk (Hsieh and Muto 2005; Hsieh and Yoshinaga 1995a, b). Consistent with previous studies in Japanese and US adult populations (Srinivasan et al. 2009; Hsieh et al. 2003, 2005), we found in this study that the W/H ratio was strongly and independently associated with individual MetS components and their clustering, especially for the cluster of high triglycerides, high BP,and low HDL-C among normal-weight Chinese adults. The mechanisms underlying the role of excess central (visceral) adiposity in the dysregulation of hemodynamic and metabolic processes may include, among others, activation of release of free fatty acids from the adipocytes, hepatic insulin resistance, lipogenesis, and ectopic lipid storage. Furthermore, the adipose renin-angiotensin system and sympathetic nervous system also contribute to these mechanisms (Kershaw and Flier 2004; Després et al. 2008).

The present epidemiologic study has certain limitations. First, we failed to compare the role of normal-weight central obesity against overweight alone because of a small number of overweight (BMI=25–29.9) subjects with the W/H ratio<0.5. Second, as a cross-sectional study, the issue of the cause-effect relationship cannot be addressed. Third, this epidemiologic study suggests only putative mechanisms for the observed relationship due to the lack of measurements of the metabolic pathways. Despite these limitations, the current study underscores the utility of the

W/H ratio in detecting asymptomatic normal-weight adults with central obesity and related adverse MetS variables. These observations have implications for prevention of MetS by controlling abdominal fat accumulation, and thus reducing CV disease risk in a population with a low level of BMI. Importantly, the index of W/H ratio may represent a potentially useful guideline for preventive health care.

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Conflict of interest The authors declare that they have no conflict of interest.

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