Characteristics of Obesity and Its Related Disorders in China[1]

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Abstract Obesity is a medical condition with excess body fat accumulation to the extent which leads to serious health consequences. Abdominal obesity, also known as central obesity, refers to the presence of excess fat in the abdominal area. Obesity, especially abdominal obesity, contributes to many metabolic disorders including metabolic syndrome (MetS), type 2 diabetes (T2DM) and cardiovascular diseases (CVD). The incidence of obesity has increased dramatically in recent years worldwide. In China, more than one-third of adults are overweight or obese and 10%-20% of all adults are affected by MetS. The pathogenesis underlying the abdominal obesity remains unclear. The ultimate health outcome of obesity and its related metabolic disorders have prompted physicians to take aggressive treatments (lifestyle changes, pharmacological interventions and surgical therapies) before a serious consequence becomes clinically apparent. In this review, we discuss the prevalence, pathogenesis and clinic features of obesity in China.

Key words: Obesity; Metabolic syndrome; Type 2 diabetes; Cardiovascular disease

INTRODUCTION

Obesity is a medical condition with excess body fat accumulation. Abdominal obesity, also known as central obesity, refers to the presence of excess fat in the abdominal area. A correlation between obesity and the risks of type 2 diabetes (T2DM) and cardiovascular disease (CVD) has been established long before[1-2]. Epidemiological studies have demonstrated that obesity, especially abdominal obesity, is associated with many metabolic disorders, such as impaired glucose tolerance, hypertension, dyslipidemia and proinflammatory status. Thus, obesity is considered to be a central component of metabolic syndrome (MetS)[3-5]. With the rapid development and globalization of the world economy, the obesity and obesity-related diseases are increasing dramatically and becoming the major public health concern in both developed and developing countries. It has been reported that one of five people with obesity in the world is Chinese[6]. Furthermore, there are distinct elements of obesity as it relates to Chinese people. This review discusses the prevalence of obesity and its related outcomes, and characterizes some features of obesity in Chinese people.

The Epidemiology of Obesity in Chinese

Over the past decade, there has been an epidemic of obesity world-wide. In the USA, two-thirds of the adult population are overweight with body mass index (BMI)$\geqslant$25 kg/m^2, and one-third are actually obese (BMI$\geqslant$30 kg/m^2)[7]. Similarly, in most European and other developed countries, more than one half of the adults are overweight or obese[8]. MetS also becomes, therefore, a global epidemic, with obesity as one of its major components. In USA, MetS nearly affects more than 20% of adults[9]. Although China is a developing country, its current rapid urbanization and economic development have led to dramatic changes in lifestyle. For example, caloric intake is significantly increased whereas physical activity is substantially reduced. These unhealthy lifestyles are all likely to contribute to the drastic increase in metabolic diseases, such as obesity, MetS, and T2DM. Two epidemiologic studies recently conducted clearly demonstrates that overweight and obesity have significantly increased in Chinese urban and rural populations during the past two decades[10-11]. A nationwide survey in China on 239 972 subjects during 1990-2000 had shown that the prevalence of

[1]This work was supported by the Major Program of Shanghai Municipality for Basic Research (08dj1400601), Shanghai Pujiang Program (07pj14062), Chinese National 973 Project (2007CB914702), and Project for Shanghai Key Laboratory of Diabetes Mellitus (08DZ2230200).

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0895-3988/2010
CN 11-2816/Q
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overweight was 22.4%, and the prevalence of obesity was 3.01% (by WHO definition in adults), respectively[12]. Mean while, we also conducted a cross-sectional study in Shanghai on 2 776 randomly selected adults (20-94 years of age) living in the community, and showed that the prevalence of overweight was 29.5% and obesity was 4.3% with a greater number of women being obese than that of men[13]. More than one-third of the obese subjects in this study were abdominally obese with waist-hip ratio over 0.9 for men and 0.85 for women[13]. After an average of 3.6 year-follow-up, the BMI in adults, especially in the group of 35-44 years age, increased significantly[14]. Positive family history of obesity increased the risk of overweight and obesity by about 1.2-fold for both genders. Current alcohol drinkers and low-education level were the risk factors for the overweight and obesity in men and women respectively[14]. Similarly, obesity is also a serious health problem in rural areas in China. In 2004, a cross-sectional whole-population health survey was undertaken in rural areas of Tianjin[15], finding that the prevalence of overweight or obesity was relatively high in the Chinese rural population, and the age-standardized prevalence of overweight and obesity was 30.0% and 8.4%, respectively. This prevalence of overweight/obesity in Tianjin was even higher than that in some other urban areas reported by the Fourth National Nutritional Survey conducted in 2002[16]. The situation could be due to more significant changes of economic and living conditions in this region[15].

It should be noted that the obesity-related metabolic disorders are common, although the prevalence of obesity is lower in China (about 4%-8%) compared with that of western countries (10%-25%). In this regard, the major epidemiological studies conducted on the prevalence of MetS in China adopted different definitions (supplement table)[17-23]. The age-adjusted MetS prevalence from our previous Shanghai community studies was 17.14% by WHO definition and 10.95% by the National Cholesterol Education Program Adult Treatment Panel III (NECP III) (2001) definition, respectively[17-18]. We showed that the WHO and NECP III (2001) definition shared 45.17% of cases of MetS. The WHO definition can better reflect the characteristics of MetS in Chinese population than the definition proposed by NECPIII (2001). A study with 16 342 subjects in Beijing showed that the age-standardized prevalence of MetS was 13.2% according to Chinese Diabetes Society (CDS) definition[19]. During 2000-2001, Yang *et al*. evaluated the prevalence of MetS with International Diabetes Federation (IDF) and revised NECPIII (2001) definitions of MetS in a nationally representative sample of 15 540 Chinese adults aged 35 to 74 years[20]. They found the age-standardized prevalence of the MetS was 16.5 % with the IDF definition and 23.3% with the revised NECP III (2001) definition. The prevalence increased with age and was higher in woman than in men. In all these studies (Table 1), it was noticed that the frequency of

TABLE 1

Standardized Prevalence of the Metabolic Syndrome according to the Different Definition in Chinese Population

		WHO (1999)	NCEP-ATPIII (2001)	NCEP-ATPIII (2005)	IDF (2005)	CDS (2004)	Ref
Shanghai	Total	17.14	10.95*	—	—	—	18.
20-74 years	Male	18.36	8.77*	—	—	—	
(*n*=2 048)	Female	15.82	13.3*	—	—	—	
Shanghai	Total	—	8.62*	—	12.81	10.41	23.
15-74 years	Male	—	7.72*	—	10.93	11.81	
(*n*=14 327)	Female	—	9.57*	—	14.79	8.94	
Beijing	Total	—	8.6*	—	—	12.2	19.
20-90 years	Male	—	9.9*	—	—	14.2	
(*n*=16 342)	Female	—	7.1*	—	—	10	
Beijing	Total	—	30.5*	36.8*	46.3	—	22.
60-95 years	Male	—	17.6*	23.2*	34.8	—	
(*n*=2 334)	Female	—	39.2*	46.1*	54.1	—	
Anhui	Total	—	7.9	—	7.2	—	21.
25-64 years	Male	—	4.9	—	3.9	—	
(*n*=18 630)	Female	—	11.5	—	10.9	—	
A nationally representative Sample	Total	—	13.7	23.3	16.5	—	20.
35-74 years	Male	—	9.8	17.7	10	—	
(*n*=15 540)	Female	—	17.8	29.1	23.3	—	

Note. *Waist circumference values are not ethnicity specific for Chinese people. Waist circumference≥102 cm for men and ≥88 cm for women.

SUPPLEMENT TABLE

Different Definition of the Metabolic Syndrome

	WHO (1999)	NCEP-ATPIII (2001)	NCEP-ATPIII (2005)	IDF (2005)	CDS (2004)	JCDCG (2007)
Required Conditions	T2DM, impaired glucose tolerance (IFG, IGT), or insulin resistance[a]	-	-	Central obesity[c]	-	-
Criteria	Required conditions plus≥2 of the following conditions	≥3 of the following conditions	≥ 3 of the following conditions	Required conditions plus ≥ 2 of the following conditions	≥3 of the following conditions	≥ 3 of the following conditions
Obesity	BMI>30 kg/m^2 and/or WHR >0.90 (M), >0.85 (F)	Waist circumference ≥ 90 cm (M), ≥ 80 cm (F)[b]	Waist circumference ≥ 90 cm (M), ≥80 cm (F)[b]	Waist circumference ≥90 cm (M), ≥80 cm (F)[d]	BMI≥25 kg/m^2	Waist circumference>90 cm (M), >85 cm (F)
Dyslipidemia I	TG ≥ 1.70 mmol/L and/or HDL-C<0.9 mmol/L (M), <1.0 mmol/L (F)	TG≥1.70 mmol/L	TG ≥ 1.70 mmol/L or drug treatment	TG>1.70 mmol/L or drug treatment	TG≥1.70 mmol/L or HDL-C<0.9 mmol/L (M), <1.0 mmol/L (F)	TG≥1.70 mmol/L
Dyslipidemia II	-	HDL-C <1.03 mmol/L (M), <1.29 mmol/L (F)	HDL-C<1.03 mmol/L (M), <1.29 mmol/L (F) or drug treatment	HDL-C<1.03 mmol/L (M), <1.29 mmol/L (F) or drug treatment	-	HDL-C <1.04 mmol/L
Hypertension	SBP/DBP≥140/90 mmHg	SBP/DBP ≥ 130/85 mmHg	SBP ≥ 130 mmHg or DBP ≥ 85 mmHg or antihypertensive treatment	SBP ≥ 130 mmHg or DBP≥85 mmHg or drug treatment	SBP/DBP ≥ 140/90 mmHg and/or drug treatment	SBP/DBP≥130/85 mmHg
Hyperglycemia	FPG≥6.1 mmol/L and/or 2 h PG≥7.8 mmol/L and/or drug treatment	FPG≥6.1 mmol/L or diabetes	FPG ≥ 5.6 mmol/L or drug treatment	FPG ≥ 5.6 mmol/L or diagnosed T2DM	FPG ≥ 6.1 mmol/L and/or 2 h PG≥7.8 mmol/L and/or drug treatment	FPG≥6.1 mmol/L and/or 2 h PG ≥ 7.8 mmol/L and/or diabetes
Microalbuminuria	urinary albumin excretion rate ≥20 μg/min or albumin: creatinine ratio≥30 mg/g	-	-	-	-	-

Note. [a]Under hyperinsulinemic euglycemic conditions, glucose uptake below lowest quartile for background population under investigation. [b]Waist circumference values are ethnicity specific for Chinese adult. [c]If body-mass index is over 30 kg/m^2, central obesity can be assumed and waist circumference does not need to be measured. [d]Lower waist circumference cut-off points appears to be appropriate for Asian Americans.

the syndrome differed according to the different definitions and the different regions in China. All these epidemiological studies indicates that the MetS has become very common in China, which will have important public health implications.

Similarly, a high prevalence of T2DM and CVD is also observed in Chinese population. Our Shanghai Diabetes Studies (SHDS)[24] found that the age-standardized prevalence was 6.87% for diabetes and 8.53% for impaired glucose regulation (IGR) at the baseline. The incidence per year of diabetes and of IGR was 1.65% and 3.7%, respectively, suggesting that the prevalence and incidence for diabetes or IGR have dramatically increased in Chinese urban population. Moreover, the patients of diabetes and IGR tend to be younger. The high presence of obesity and MetS also increase the likelihood of the occurrence of CVD. Data from the Sino-MONICA project reported by Wu *et al*. showed that the incidence of coronary heart disease (CHD) reached 108.7 per 100 000 people (1987 to 1989), and the incidence of cerebrovascular disease reached 553.3 of 100 000 people (1987 to 1989)[25]. CVD is now the major cause of death in China. Among the deaths caused by CVD, stroke and CHD accounted for 77%[26]. In contrast to the decline among western populations, the death rate from CHD has been on the rise in China in the recent years[27]. We are facing a big challenge.

The Feature of Obesity in Chinese

BMI, as a measurement of obesity, is easy to obtain and use in clinic. At present, there has been many researches on defining the appropriate BMI cut-off point for obesity in Asian population[28-29]. Studies have demonstrated that the increased risks of T2DM and CVD associated with obesity occur at lower BMIs in Asians. Therefore, a lower BMI cut-off point should be recommended in the prediction of risk of T2DM and CVD for Chinese people, compared with the international BMI cut-off points (30 kg/m^2) recommended by the WHO[30-31]. In this regard, BMIs of 24 kg/m^2 and 28 kg/m^2 were proposed as cut-off points for overweight and obesity Chinese people, respectively[30,32]. This was confirmed by subsequent studies, in which BMI$\geqslant$24 kg/m^2 demonstrated to be a more appropriate cut-off point in identifying overweight in Chinese population[33-34].

Studies have also shown that Asian populations are predisposed to visceral or abdominal obesity than Caucasians[35-37]. There has been a general trend that Chinese people with obesity tend to be apple-shaped (abdominal obesity) rather than pear-shaped (generalized obesity)[38]. Compared with the increase in total body fat (reflected by BMI), the excess of body fat in the abdomen is more closely related to the metabolic disorders. The IDF in 2005 also stressed the prerequisite role of abdominal obesity in MetS[39]. The IDF group has recommended that the accumulation of abdominal fat should be determined by visceral fat area (VFA) precisely measured by the magnetic resonance imaging (MRI) or computed tomography (CT). We showed in our previous cross-sectional study including 1 140 subjects that VFA over 80 cm^2 linked with high prevalence of MetS in Chinese, and in those with VFA over 80 cm^2 the frequency of the MetS had nearly reached the plateau[33]. This value (80 cm^2) was lower than those reported by Japan (100 cm^2) and Korea (103.8 cm^2)[40-41].

Though MRI or CT scanning is a widely accepted measurement of abdominal obesity, the inconvenience and high cost limit the 'platinum standard' measurement in clinical use and epidemiological survey. Waist circumference, a simple clinic and noninvasive measurement, is used as a surrogate marker for abdominal fat mass to discriminate for the presence of abdominal obesity. Our previous study confirmed that waist circumference had an excellent correlation with VFA. In terms of sensitivity and specificity, waist circumference was the one with better accuracy for measuring abdominal obesity and in diagnosing abdominal obesity in Chinese adults, compared with BMI[42]. However, there is a great variability of links between abdominal fat accumulation and the risk of MetS among different populations, ethnicities, nationalities and genders. The IDF proposed that the values for waist circumference should be ethnic-group specific, and consequently waist circumference of 90 cm and 80 cm were defined as the cut-off of abdominal obesity for Chinese men and women, respectively. We showed in our previous survey with Chinese community population that before age of 60, the difference of waist circumference between men and women was about 5 cm regardless of different mean waist circumference values within different age group, and no difference could be found in waist circumference between the two genders after 60[13]. The result suggested that the IDF criteria might not be suitable for Chinese. In Asians, numerous studies have been performed to find the optimal cut-off points of waist circumference for defining abdominal obesity. To find the appropriate cut-off points for obesity linking to risk of MetS in Chinese people, Bao *et al*. performed a cross-sectional study[33] showing that in terms of estimation of abdominal fat, a waist circumference of 87.5 cm in men and 84.3 cm in women approximated

to the 80 cm^2 cutoff point of VFA detected by MRI, were the effective indicators of the risk of obesity-related disorders in Chinese population. Our waist circumference cut-off points were similar with those reported by Oka *et al*. (90 cm for Japanese men and 82 cm for women), and those reported by Han *et al*. (88 cm for Korean men and 84 cm for women) in 2008[43-44]. Thus, the waist circumference of 90 cm and 85 cm in men and women, respectively, might be the suitable cutoff points for determining abdominal obesity in Asians. Furthermore, the 90 cm and 85 cm of waist circumference in men and women were corresponding to a BMI of 25 kg/m^2 [33].

Given the evidence on the optimal waist circumference for abdominal obesity in Chinese population mentioned above, the Chinese Joint Committee for Developing Chinese Guidelines on Prevention and Treatment of Dyslipidemia in Adults (JCDCG) proposed a new set of criteria to define the MetS in 2007[45]. In the revised definition, the waist circumference cut-off points of 90 and 85 cm were suggested for Chinese men and women to detect abdominal obesity. In 2009, we carried out an analysis of the effect of abdominal obesity on predicting diabetes in a 7.8-year follow-up study in the Chinese population. The results reported that the visceral obesity significantly increased the risk of future diabetes. The corresponding cut-off points of waist circumference were 88 cm for man and 82 cm for women[34]. In addition, our prospective study evaluating the predictive effect of the MetS for CVD in Chinese population demonstrated that the MetS based on the JCDCG definition was a significant predictor for the development of CVD compared with that defined by the IDF[46]. These studies further prove that the waist circumference thresholds in the definition of JCDCG are appropriate for obesity-related risk assessment in Chinese population.

Obesity, Adipokine, and Inflammation

In addition to being as an energy store, adipose tissue is recently considered as an important endocrine organ. Adipocytokines, secreted from adipose tissue, play an important role in the occurrence of obesity-related MetS and insulin resistance. Previous studies have found that adiponectin, a most abundant adipokine, modulates the energy metabolism and increased insulin sensitivity[47-48]. A population-based cross-sectional study in China showed that the prevalence and the number of MetS component increased progressively with declined adiponectin[49]. Individuals with a lower level of adiponectin were associated with significantly increased risk for MetS. Moreover, it was found that leptin to adiponectin ratio and leptin might be better diagnostic markers for MetS than adiponectin. The close relationship of leptin with MetS was mediated by the obesity[50]. Additionally, several cytokines including retinol binding protein 4 (RBP4) and visfatin, may also mediate glucose and lipid metabolism and insulin sensitivity[51-52]. Further investigations deem necessary to illustrate the comprehensive pathophysiology.

C-reactive protein (CRP) is secreted by the liver in response to inflammatory cytokines. Elevated CRP is commonly present in individual with visceral obesity and risk of MetS[53-54]. Similar results are also found in Chinese population[55-56]. Two cross-sectional studies in Chinese population were conducted and showed that serum CRP level was gradually elevated with the increment of the components of metabolic disorders[57-58]. In individuals with MetS, CRP level was higher than in those with 1 or 2 components of metabolic disorders. Compared with those in the lowest quartile of CRP, Chinese people in the highest quartile of CRP had increased relative risk of MetS and its components[58]. No gender difference in CRP levels was observed[57]. It is worth noting that central obesity is a critical mediator for the relationship between CRP and MetS[59]. Studies found that higher BMI and waist circumference were closely related to elevated CRP level[60-61]. The ability of CRP to predict MetS was virtually attenuated by adjustment for BMI[57]. It is possibly because that excess adipose tissue in obese subjects releases excess cytokines, for example IL-6, that may drive higher CRP level[62].

Several studies have reported that an elevated level of CRP also plays a critical role in the development of CVD[63-64]. CRP is recommended as an additional measure to assess MetS associated CVD risk[65]. To further investigate the role of high-sensitivity CRP (hs-CRP) on the risk of MetS related-CVD, we conducted a study, in which a total of 2 656 Chinese participants were monitored for the incidence of a composite of CVD events during a 5.5-year period of follow up[66]. The study found, although the hs-CRP level was much lower in Chinese population (median 0.97 mg/L) than in western populations (median approximately 1.5-3.0 mg/L)[67], the incidence of CVD still increased progressively with the increasing quartiles of hs-CRP. The slightly elevated hs-CRP ($\geqslant$2.0 mg/L) was an effective predictor of CVD independent of the traditional risk factors of CVD. The effect was especially significant for stroke. The study proposed that a lower cut-off point of hs-CRP level in predicting the risk of CVD events be likely suitable for Chinese populations compared with Western

populations. Considering the discrepancies of CRP distribution between Chinese and Western populations, more prospective studies about the association between CRP, MetS and CVD are needed (to establish) in Chinese population.

Implications of Obesity

As discussed elsewhere above, obesity leads to serious health consequences, including MetS, T2DM, CVD, and cancer. MetS identifies a subgroup of patients with visceral adiposity, hyperglycemia/insulin resistance, hypertension, and dyslipidemia. All these elements are known to be the important CVD or T2DM risk factors. Thus, the definition of MetS has an important practical use in identifying patients at higher risk of developing CVD or T2DM. But it is not well proven. More epidemiological evidence is needed.

A meta-analysis of nearly 173 000 participants reported that the risk of incident CVD events and death were increased about 1.7-fold in people with the MetS[68]. The association remained after adjustment for traditional risk factors. It was also found the CVD risk conferred by MetS was higher in women than in men. WHO-based criteria were better than NCEP in predicting CVD events and death[68]. Results were similar in other meta-analyses[69-70].

Recently, we studied the impact of MetS on the development of CVD[46]. To evaluate the predictive value of the MetS for CVD events in Chinese population by different MetS definitions, we performed a community-based cohort study in Shanghai including 2 788 subjects to monitor the incidence of CVD events during a 5.5-year period. We used the WHO, IDF, NCEPIII and JCDCG criteria for determining MetS. All four definitions were associated with the increased risk of CVD events in women, but not in men. The hazard ratios (HRs) remained significant with WHO and JCDCG definitions, but not with the IDF and NCEPIII definitions, when factors of low-density lipoprotein cholesterol (LDL-c) and smoking were adjusted. Competitive advantage was gained in CVD risk assessment by using WHO or JCDCG. Similar result was found in other Chinese study later[71]. It is worth noting that, obesity is very important to the MetS related CVD in Chinese and Western population[72-73]. Zhao *et al*. found that 78% of Chinese patients with MetS had central obesity, which was also closely associated with other metabolic disorders and increased CVD risk[73].

MetS, regardless of how it is defined, has a close association with the incident diabetes in many different populations[74]. Among these studies, a 6-year follow-up study in Chinese population proposed that the MetS increased the risk of diabetes by about 3-fold. The absence of MetS strongly predicts the absence of future diabetes[75]. What is the potential reason for the effect of MetS on the future risk prediction of diabetes? First, the considerable effects of MetS are probably due to the components of MetS including glucose intolerance[76]. Elevated plasma glucose, by itself, is a stronger predictor of the development of diabetes[77]. Second, obesity, the central component of MetS, is also an effective risk factor for adult-onset diabetes[78-79]. An analysis of the effect of abdominal obesity on predicting diabetes in the Chinese population has reported that the visceral obesity significantly increases the risk of diabetes for 2.4-3.6 folds after about 7-year follow-up[34].

PERSPECTIVE

In summary, obesity, especially abdominal obesity, is a very important risk factor for MetS, T2DM and CVD. The lower BMI and the higher visceral fat accumulation are the characteristic features of Chinese obesity. A comprehensive understanding for the obesity is important to recognize the common pathophysiology of CVD or diabetes, and to motivate people to take appropriate interventions aimed at risk reduction of CVD and diabetes. It may also lead to the development of new pharmacological management for the composite metabolic abnormalities. Thus, further multidimensional and multidisciplinary work is urgently required to establish the feature of obesity in various populations and to control the epidemics of the obesity.

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(*Received December* 20, 2009 *Accepted January* 6, 2010)