

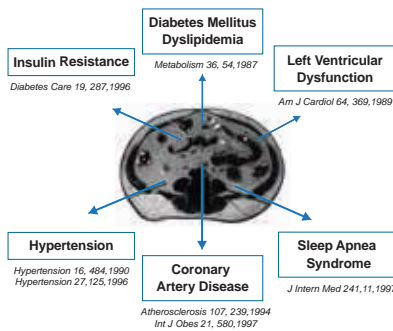


Abdominal Obesity in Asia: Current Trends

Written by Mary Mosley

Visceral fat accumulation (VFA) has been correlated with the development of many common diseases, including type 2 diabetes mellitus (T2DM; Figure 1), and has been shown to be a more important contributor than body mass index (BMI) to obesity-related metabolic risk factors [Okauchi Y et al. *Diabetes Care* 2007].

Figure 1. Visceral Fat Accumulation Contributes to Disease Development



Kanai H et al. *Hypertension* 1990; Kanai H et al. *Hypertension* 1996; Nakamura T et al. *Atherosclerosis* 1994; Nakamura T et al. *Int J Obes Relat Metab Disord* 1997; Shinohara E et al. *J Intern Med* 1997.

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Gene expression profiling of human adipose tissue through the BODYMAP project revealed adipose tissue, especially visceral fat contains growth factors, cytokines, and complement factors, among others, that have been associated with the development of atherosclerosis [Maeda K et al. *Gene* 1997]. Adiponectin may be the most important gene identified by the BODYMAP program, said Yuji Matsuzawa, MD, PhD because it has been hypothesized to be protective and associated with less insulin resistance, vascular stenosis, thrombosis, and inflammation.

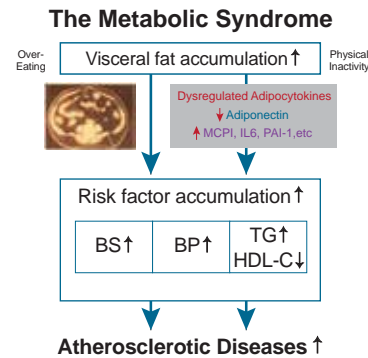
VFA is a key player in the metabolic syndrome (MetS) inducing low adiponectin levels (ie, hypoadiponectin), which is associated with the development of T2DM, hypertension, atherosclerosis, cardiac dysfunction, and some malignancies. The precise mechanism for reduced adiponectin production by VFA is not fully elucidated although it has been hypothesized that increased production of TNF-alpha or reactive oxygen species and hypoxia may be part of the pathway.

Several lines of research have shown a relationship between insulin resistance and low plasma levels of adiponectin in mice [Maeda N et al. *Nat Med* 2002], a negative correlation between plasma adiponectin and blood pressure (BP) in humans, regardless of insulin resistance, suggesting hypoadiponectin may be involved with the development of hypertension in MetS [Iwashima

Y et al. *Hypertension* 2004]; and a close correlation between adiponectin and endothelium-dependent vasodilation [Ouchi N et al. *Hypertension* 2003].

In patients with coronary artery disease (CAD), adiponectin levels are lower than in age- and BMI-adjusted control subjects [Ouchi N et al. *Circulation* 1999]. In contrast, high levels of adiponectin were associated with a lower prevalence of cardiovascular (CV) death in chronic renal failure patients, and another study found that patients with higher adiponectin were associated with a 30% lower incidence of myocardial infarction (MI) [Kumada M et al. *Arterioscler Thromb Vasc Biol* 2003]. The possible relation between lifestyle factors, visceral fat, and atherosclerotic disease is summarized in Figure 2.

Figure 2. Visceral Fat Accumulation Leads to Atherosclerosis



BP=blood pressure; BS=blood sugar; HDL-C=high-density lipoprotein cholesterol; TG=triglycerides.

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TRENDS IN METABOLIC SYNDROME AND DIABETES IN KOREA

Soo Lim, MD, PhD, Seoul National University College of Medicine, Seoul, South Korea, presented data from 3 national studies he conducted with his colleagues to characterize the prevalence of MetS and diabetes in Korea.

The Korea Genomic Epidemiology Study (KOGES) began in 2001 and has enrolled approximately 10,000 Korean subjects aged 40 to 70 years with MetS (defined using the NCEP-ATP III criteria modified for waist circumference [>90 cm for men, >80 cm for women]) [Lim S et al. *J Endocrinol Invest* 2006]. The overall prevalence of MetS was 26.1% (20.0% in men and 31.7% in women). Menopause may account for the sex difference, said Prof. Lim. Of the 5 components of MetS, abdominal obesity (AO; high waist circumference) comprised the highest proportion contributing to MetS (55.9%), followed by low HDL-C at 49.4%, BP 34.3%, triglycerides (TG) 30.5%, and glucose 10.3%. A clear relationship between AO and an

inflammatory process was found, with a significant association between AO and increased levels of the inflammatory marker C-reactive protein (OR, 2.36).

The Korean National Health and Nutrition Examination Survey (KNHANES), using the 2004 NCEP-ATP III criteria modified for waist circumference, found the prevalence of MetS increased from 22.2% in 1998 (mean age 45 years; n=6907) to 31.5% in 2007 (mean age about 50 years; n=2890) [Lim S et al. *Diabetes Care* 2011]. The prevalence of MetS increased with age, and it was higher in women than in men particularly in older ages. The leading causes of the increasing trend of MetS in Korea were AO, high TG and low HDL-C.

Prof. Lim and colleagues investigated the prevalence of MetS in children and adolescents in the United States and Korea using NHANES data and a modified 2009 NCEP-ATP III criteria (waist circumference \geq 90th percentile for age and sex; serum TG \geq 100 mg/dL; HDL-C \leq 40 mg/dL, high BP \geq 90th percentile for age, sex, and height or current use of BP medication; fasting glucose \geq 110 mg/dL or current antidiabetic medication). Notably, there was a 95% increase in the prevalence of MetS from 1998 to 2007 in Korean youth (4.0% in 1998; 7.8% in 2007) [Lim S et al. *Pediatrics* 2013]. In contrast, the prevalence of MetS decreased by 11% in US youth during this time period (7.3% in 1988-1994; 6.5% in 2003-2006).

This increase in MetS in Korean adolescents was driven by high TG, low HDL-C, and high waist circumference, stated Prof. Lim, and the reduction in US adolescents was driven by improvements in BP and HDL-C. Furthermore, he stated the rapid economic development in Korea has been accompanied by a high-calorie, high-fat diet, plus low physical activity, which have contributed to the increase in MetS. The proportion of fat in the daily calorie intake significantly increased from 7.2% in 1969 to 20.3% in 2005.

AO leads to a pathological accumulation of excess adipose tissue in various organs, and this ectopic fat deposition may lead to cardiometabolic disorders and other organ-specific diseases, stated Prof. Lim.

TRENDS IN CHINA IN METABOLIC SYNDROME AND DIABETES

An extensive study of 98,658 subjects from all 31 Chinese provinces by the Chinese Centers for Disease Control reported in 2013 provided new insights into the prevalence of MetS, diabetes, and prediabetes in China [Xu Y et al. *JAMA* 2013]. Fasting plasma glucose (FPG), 2-hour plasma glucose (PG), and HbA1C $<$ 6.5% were used to diagnose diabetes and prediabetes. The majority of diabetes was detected by FPG (sensitivity) and HbA1C (specificity) in this study, thus confirming their utility to identify high-risk persons, said Juliana C. Chan, MD, Hong Kong Institute of Diabetes and Obesity, Hong Kong.

In 2007, the estimated prevalence rates of T2DM was 11% and prediabetes 15% as determined from 4000 people in 21 Chinese provinces. In the 2013 study, 10% to 15% of

men and women, urban or rural living, had T2DM, and nearly 50% had prediabetes. There was a tendency for the increase in T2DM to be higher in the more affluent areas. Of persons aged $<$ 30 years, 5% had T2DM and 40% had prediabetes. After the age of 50, there was a tendency for women to catch up in the rate of T2DM, while there was little sex difference in prediabetes.

In a sample of 100,000 Chinese people in the CDC study, 30 to 35% were overweight, obese, or had central obesity. Of the obese persons, 25% had prediabetes and 10% had diabetes. In the obese population, 1 out of 5 subjects had T2DM. The prevalence of obesity was 2- to 3-times higher among those with central obesity. Nearly 14% of subjects had either a high fasting glucose or HbA1C between 5.5% and 6.5%. There was a direct relationship between increasing weight and the risk of diabetes. Obesity (OR, 2.03), central obesity (OR, 1.64), and being overweight (OR, 1.31) were all associated with the presence of diabetes in the 2013 study (Table 1).

Table 1. Clustering of Risk Factors and Impact on Diabetes and Prediabetes

	Diabetes		Prediabetes	
	OR	p Value	OR	p Value
Weight				
Overweight	1.31 (1.21–1.41)	$<$ 0.001	1.19 (1.12–1.25)	$<$ 0.001
Obesity	2.03 (1.78–2.32)	$<$ 0.001	1.52 (1.37–1.70)	$<$ 0.001
Central obesity	1.64 (1.51–1.77)	$<$ 0.001	1.17 (1.11–1.24)	$<$ 0.001
Physical activity per 105 MET, h/wk	0.99 (0.96–1.02)	0.53	1.06 (1.04–1.08)	$<$ 0.001
SBP per 22 mm Hg	1.47 (1.42–1.52)	$<$ 0.001	1.17 (1.14–1.20)	$<$ 0.001
Cholesterol				
Total per 43 mg/dL	1.65 (1.47–1.85)	$<$ 0.001	1.61 (1.46–1.76)	$<$ 0.001
LDL per 31 mg/dL	1.10 (1.01–1.20)	0.03	0.97 (0.91–1.04)	0.46
HDL per 12 mg/dL	0.70 (0.66–0.73)	$<$ 0.001	0.79 (0.76–0.82)	$<$ 0.001
Triglycerides per 118 mg/dL	1.12 (1.07–1.18)	$<$ 0.001	0.93 (0.89–0.97)	0.002
Intermediately developed vs underdeveloped	0.80 (0.74–0.87)	$<$ 0.001	0.77 (0.74–0.81)	$<$ 0.001
Developed vs underdeveloped	1.00 (0.92–1.09)	0.93	0.89 (0.84–0.94)	$<$ 0.001

The rate of smoking was high; 1 in 2 Chinese men were smokers. A meta-analysis showed that smoking was associated with a 44% increased risk of diabetes [Willi C et al. *JAMA* 2007].

Prof. Matsuzawa noted that in Japan the prevalence of MetS decreased from 2006 to 2008, as a result of an aggressive national public health campaign. In 2008, 29.6% of obese men and 21.7% of obese women had MetS.