Ten-year risk of cardiovascular incidence related to diabetes, prediabetes, and the metabolic syndrome

Jing Liu, MD,[a,b] Scott M. Grundy, MD, PhD,[b] Wei Wang, MD,[a] Sidney C. Smith Jr, MD,[c] Gloria Lena Vega, PhD,[b] Zhaosu Wu, MD, MPH,[a] Zhechun Zeng, MD,[a] Wenhua Wang, MD,[a] and Dong Zhao, MD, PhD[a]
Beijing, China; Dallas, TX; and Chapel Hill, NC

Background The relative contributions of the metabolic syndrome (MetS) and dysglycemia on the risk of cardiovascular disease (CVD) have not been dissected. We aimed to compare MetS with dysglycemia in their association with the 10-year incidence risk of CVD.

Methods A total of 30378 subjects were recruited from 11 provinces in the CMCS and followed-up for new coronary heart disease (CHD) and stroke events (ischemic stroke and hemorrhagic stroke) for 10 years. Incidence rates and HRs were estimated by the presence or absence of MetS, impaired fasting glucose (IFG) and diabetes, and by the various traits of MetS.

Results Among the subjects, 18.2% were defined as having MetS; 21.1% had IFG, and 6.8% had diabetes. Metabolic syndrome prevalence in IFG and diabetes was 38.1% and 48.7%, respectively, and the prevalence of IFG and diabetes in MetS was 44.1% and 18.3%, respectively. After adjusting for nonmetabolic risk factors, HRs of total CVD, CHD, and ischemic stroke in MetS were significant and higher than those in non-MetS, regardless of glycemic status. In the absence of MetS, the impact of dysglycemia was found only in IFG to CHD and diabetes to ischemic stroke. Hyperglycemia without any concomitant disorders was not associated with significantly higher risk of CVD.

Conclusions The increased CVD risk in individuals with IFG or diabetes was largely driven by the coexistence of multiple metabolic disorders rather than hyperglycemia per se. Identification of clustering of metabolic abnormalities should be given more consideration in CVD prevention. (Am Heart J 2007;153:552-8.)

The mortality of cardiovascular disease (CVD) has fallen in many countries, but it has been rising in China in recent decades, accompanying the rapid change in lifestyle, such as unhealthy diet and physical inactivity.[1] Cardiovascular disease is now the leading cause of death in China, accounting for >40% in total mortality.[2] Well-established risk factors for CVD are smoking, dyslipidemia, hypertension, and dysglycemia. An important condition underlying the latter 3 is obesity, which is becoming increasingly common in China.[3] The clustering of these risk factors has been called the metabolic syndrome (MetS).[4]

Because impaired glucose regulation closely interplays with other components of MetS, and elevated glucose per se is considered as one of the components in the clinical definition of MetS, to date, the CVD risk associated with MetS versus elevated glucose independent of each other has not been fully defined.[5] Several studies have demonstrated that people with MetS had an increase in CVD prevalence, incidence, or mortality even without diabetes.[6-8] On the other hand, the isolated effect of diabetes on CVD is less studied. Alexander et al[6] reported that in the NHANES III, people with diabetes without MetS did not have an increase in coronary heart disease (CHD) prevalence; nevertheless, the follow-up study of NHANES II showed diabetes independent of MetS carries an increased risk for CHD and CVD mortality.[8] To compare and contrast the CVD risk associated with the MetS and impaired glucose regulation independent of each other, we evaluated the 10-year incidence risk of different types of CVD (including CHD, ischemic stroke, and hemorrhagic stroke) in relation to MetS and dysglycemia (impaired fasting glucose [IFG] and diabetes) in the Chinese Multi-provincial Cohort Study (CMCS).

From the [a]Capital Medical University attached Beijing Anzhen Hospital, Beijing, China, [b]Center for Human Nutrition, University of Texas Southwestern Medical Center, Dallas, TX, and [c]Center for Cardiovascular Science and Medicine, University of North Carolina School of Medicine, Chapel Hill, NC.
This research was supported by the China National Grant on Science and Technology (85-915-01-02), China fundings from Beijing Municipal Bureau of Science and Technology (953850700) (Beijing, China), and Beijing NOVA Program (2003B26) (Beijing, China).
Submitted August 8, 2006; accepted January 4, 2007.
Reprint requests: Dong Zhao, MD, PhD, Department of Epidemiology, Capital Medical University attached Beijing Anzhen Hospital, Beijing Institute of Heart, Lung and Blood Vessel Diseases, Beijing 100029, China.
E-mail: deezhao@anzhen.org
0002-8703/$ - see front matter

doi:10.1016/j.ahj.2007.01.003

Methods

Subjects

The CMCS was a nationwide, multicenter, prospective cohort study on CVD. As previously reported,[9,10] a total of 30 378 subjects 35 to 64 years of age and free of CVD were included with the informed consent. Ninety percent of the participants (n = 27 249) were recruited from the baseline survey in 1992, carried out in 16 centers from 11 provinces of China. In addition, 3129 subjects from Beijing were added in 1996 to 1999. The response rate was 82.1% and 75.0% for the 2 surveys, respectively. Both surveys followed the protocol in the WHO-MONICA Project.[11] A face-to-face follow-up for new CHD and stroke events was carried out at the end of each year for the 1992 cohort from 1992 to 1995, and the follow-up rate was 94%. From 1996, 6 centers ceased following up because of the completion of that national research project. The remainder 16 811 subjects in 10 centers of the 1992 to 1993 cohort and the 3129 subjects of the 1996 to 1999 cohort were continuously followed up till the end of 2003, and the follow-up rate was 86%.

Ascertainment of CHD and stroke

Coronary and stroke events were ascertained according to the WHO-MONICA protocol.[11,12] Coronary events include acute myocardial infarction, sudden death, and other coronary deaths. The events were diagnosed based on symptoms, development in ECG (Minnesota codes for up to 4 records), serum enzymes, and autopsy findings. Stroke events included patients presenting with clinical signs and symptoms suggestive of subarachnoid hemorrhage, intracerebral hemorrhage, or cerebral infarction, which were defined as rapidly developing signs of focal (or global) disturbance of cerebral function lasting >24 hours (unless interrupted by surgery or death) with no apparent nonvascular cause. Detailed procedure of case registration and quality control has been published elsewhere.[11-13]

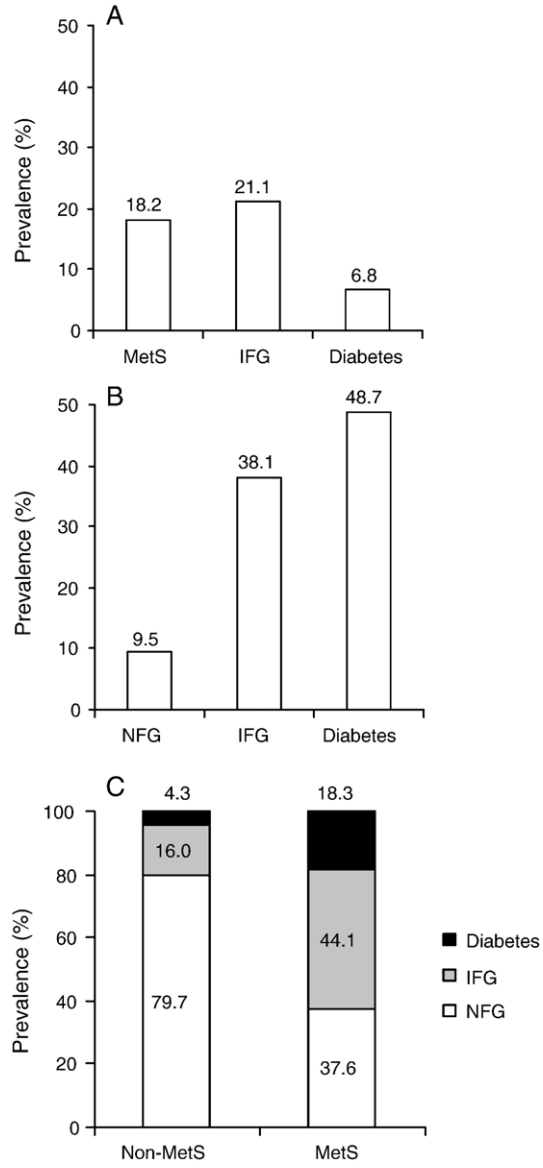
Definition of diabetes, IFG, and the MetS

Diabetes was diagnosed if fasting blood glucose ≥126 mg/dL (7.0 mmol/L) at the baseline examination as defined by the American Diabetes Association (ADA)[14] or with a previous clinical diagnosis. Impaired fasting glucose was defined when fasting glucose ranged from 100 to 125 mg/dL.[14] The MetS was defined according to the updated criteria from the Third Adult Treatment Panel Report of the National Cholesterol Education Program,[4] which requires the presence of ≥3 of the following: elevated triglyceride (TG) level ≥150 mg/dL, reduced high-density lipoprotein cholesterol (HDL-C) (men <40 and women <50 mg/dL), elevated fasting glucose ≥100 mg/dL or previously diagnosed diabetes, elevated blood pressure (BP) (systolic BP ≥130 mm Hg and/or diastolic BP ≥85 mm Hg or on antihypertensive medication), or large waist circumference for Asians (≥90 cm in men and ≥80 cm in women). Evidence to support these waist thresholds to define abdominal obesity for the Chinese population has been recently reported.[15]

Statistical analysis

The prevalence rates of risk factors were adjusted for age and sex and stratified by glycemic status and presence or absence of the MetS. Incidence rates were calculated by dividing the number of events occurred by person-years of follow-up. Multivariate Cox proportional hazards models were fitted to assess the hazard ratios of CVD incidence in relation to diabetes, IFG, and the MetS and adjusted for age, sex, smoking, CVD family history, and elevated total cholesterol. The interaction with sex was tested at a probability of .05, and no statistical significant interaction was found. SPSS software (Version 13; SPSS, Chicago, IL) was used for all analysis.

Figure 1



Prevalence of the MetS and dysglycemia. **A**, Prevelance of MetS, IFG, and diabetes; **B**, prevelance of MetS in subjects with NFG, IFG, and diabetes; **C**, prevelance of NFG, IFG, and diabetes in subjects with or without MetS.

Results

This study revealed the interrelations of MetS and dysglycemia in the middle-aged Chinese population.

Table I. The characteristics of subjects categorized by the presence of the MetS and glycemic status

	Without MetS			With MetS		
	NFG	IFG	Diabetes	NFG	IFG	Diabetes
No. of subjects (%)	19805 (65.2%)	3973 (13.1%)	1066 (3.5%)	2081 (6.9%)	2442 (8.0%)	1011 (3.3%)
Sex (male) (%)	53.8	58.6	62.2	40.3	50.2	53.4
Age (y)	46.1 (46.0-46.2)	46.4 (46.1-46.6)	47.6 (47.2-48.1)	49.5 (49.2-49.9)	49.6 (49.3-49.9)	51.4 (50.9-51.9)
Smoking	22.2 (21.6-22.8)	16.4 (15.2-17.6)	17.9 (15.6-20.2)	21.2 (19.4-23.0)	15.4 (14.0-16.8)	17.8 (15.4-20.2)
CVD family history	20.3 (19.7-20.9)	21.7 (20.4-23.0)	24.2 (21.6-26.8)	26.9 (25.0-28.8)	26.3 (24.6-28.0)	28.1 (25.3-30.9)
Total cholesterol ≥200 mg/dL	29.1 (28.5-29.7)	32.4 (30.9-33.9)	30.4 (27.6-33.2)	36.3 (34.2-38.4)	38.2 (36.3-40.1)	40.5 (37.5-43.5)
LDL-C ≥130 mg/dL	22.2 (21.6-22.8)	24.4 (23.1-25.7)	23.3 (20.8-25.8)	26.5 (24.6-28.4)	28.1 (26.3-29.9)	28.3 (25.5-31.1)
HDL-C <40/50 mg/dL	15.5 (15.0-16.0)	9.5 (8.6-10.4)	11.4 (9.5-13.3)	72.4 (70.5-74.3)	46.8 (44.8-48.8)	49.8 (46.7-52.9)
Non HDL-C ≥160 mg/dL	17.4 (16.9-17.9)	18.1 (16.9-19.3)	16.6 (14.4-18.8)	34.0 (32.0-36.0)	31.4 (29.6-33.2)	33.0 (30.1-35.9)
TG ≥150 mg/dL	13.4 (12.9-13.9)	8.0 (7.2-8.8)	6.8 (5.3-8.3)	74.2 (72.3-76.1)	51.2 (49.2-53.2)	56.2 (53.1-59.3)
Blood pressure ≥130/85 mm Hg	29.0 (28.4-29.6)	22.2 (20.9-23.5)	22.6 (20.1-25.1)	86.3 (84.8-87.8)	74.3 (69.2-72.8)	73.6 (70.9-76.3)
Waist circumference ≥90/80 cm	19.7 (19.1-20.3)	12.6 (11.6-13.6)	12.6 (10.6-14.6)	86.0 (84.5-87.5)	71.0 (69.2-72.8)	70.8 (68.0-73.6)
Body mass index ≥25 kg/m^2	25.9 (25.3-26.5)	25.0 (23.7-26.3)	23.5 (21.0-26.0)	75.7 (73.9-77.5)	67.7 (65.8-69.6)	67.8 (64.9-70.7)
On drug treatment for hypertension	3.6 (3.3-3.8)	2.9 (2.4-3.4)	3.3 (2.2-4.3)	13.7 (12.2-15.2)	11.1 (9.9-12.4)	13.8 (11.6-15.9)
On drug treatment for dyslipidemia	0.8 (0.7-1.0)	0.6 (0.4-0.9)	0.7 (0.2-1.2)	2.3 (1.7-2.9)	2.1 (1.5-2.6)	2.4 (1.5-3.4)
The use of aspirin	0.7 (0.6-0.8)	0.6 (0.3-0.8)	0.8 (0.3-1.3)	1.0 (0.6-1.5)	1.4 (0.9-1.8)	1.8 (1.0-2.7)

Sex is presented as the percentage for men. Age is presented as means and 95% CI. All other data are presented as prevalence rate (%) and 95% CI after adjusting for age and sex. HDL-C <40/50 mg/dL indicates HDL-C <40 mg/dL in men or <50 mg/dL in women; blood pressure ≥130/85 mm Hg, systolic blood pressure ≥130 mm Hg and/or diastolic blood pressure ≥85 mm Hg or on antihypertensive medication; waist circumference ≥90/80 cm, waist circumference ≥90 cm in men and ≥80 cm in women.
LDL-C, Low-density lipoprotein cholesterol.

Table II. Incidence rates (1/100000 person years) and hazard ratios of cardiovascular diseases by different traits of dysglycemia and the MetS

Traits of dysglycemia and MetS	% of subjects	CVD (CHD + stroke)		CHD		Ischemic stroke		Hemorrhagic stroke	
		Incidence	HR (95% CI)	Incidence	HR (95% CI)	Incidence	HR (95% CI)	Incidence	HR (95% CI)
Glycemic status									
NFG	72.1	350.3	Reference	100.9	Reference	176.5	Reference	79.9	Reference
IFG	21.1	497.0	1.29 (1.10-1.51)	158.1	1.42 (1.06-1.89)	271.1	1.39 (1.12-1.73)	76.8	0.88 (0.60-1.30)
Diabetes	6.8	700.8	1.66 (1.33-2.09)	220.5	1.81 (1.20-2.71)	441.0	2.06 (1.54-2.76)	78.7	0.84 (0.44-1.60)
MetS status									
Non-MetS	81.8	323.7	Reference	101.1	Reference	159.7	Reference	67.2	Reference
MetS	18.2	757.0	2.01 (1.73-2.33)	207.9	1.80 (1.36-2.37)	450.5	2.41 (1.98-2.94)	130.6	1.63 (1.16-2.30)
Number of MetS components									
0	26.9	141.8	Reference	67.9	Reference	55.9	Reference	18.0	Reference
1	31.7	295.5	1.84 (1.40-2.42)	70.3	0.93 (0.59-1.45)	151.9	2.39 (1.57-3.64)	73.4	3.65 (1.79-7.46)
2	23.2	548.6	3.19 (2.45-4.16)	173.7	2.20 (1.47-3.28)	274.8	4.01 (2.66-6.03)	107.9	4.97 (2.44-10.10)
3	12.6	709.3	3.96 (3.00-5.22)	171.4	2.08 (1.33-3.27)	449.0	6.27 (4.14-9.51)	114.0	5.01 (2.36-10.61)
4	4.6	782.0	4.28 (3.08-5.95)	215.7	2.59 (1.49-4.50)	425.6	5.84 (3.59-9.50)	153.6	6.56 (2.84-15.15)
5	1.0	1260.7	6.76 (4.27-10.71)	598.4	7.08 (3.63-13.80)	545.5	7.39 (3.66-14.91)	196.0	8.35 (2.55-27.35)

Cardiovascular diseases include coronary heart disease and stroke.

Among the subjects, 18.2% were defined as having MetS, 21.1% had IFG, and 6.8% had diabetes (Figure 1). The prevalence of MetS in IFG and diabetes was 38.1% and 48.7%, 4.0 and 5.1 times of that in subjects with normal fasting glucose (NFG), respectively. Sixty-two percent of the subjects with MetS had IFG or diabetes, which was 3.1 times of that prevalent in non-MetS. After adjustment for age and sex, the risk factor levels were higher in subjects with the MetS regardless of glucose levels, except for smoking (Table I). Another potentially important finding was a strikingly higher prevalence of elevated non–HDL-C in persons with MetS.

Table III. Incidence rates (1/100000 person years) and hazard ratios of total cardiovascular disease by different MetS traits

MetS traits	% of subjects	No. of cases	Incidence	HR (95% CI)	P
None	26.9	71	141.8	Reference	NA
1 component					
TG	4.0	11	122.5	0.64 (0.34-1.22)	.174
Waist	5.1	16	164.3	1.16 (0.67-2.03)	.600
GLU	7.4	30	208.9	1.32 (0.86-2.02)	.206
HDL-C	5.2	18	167.8	1.53 (0.90-2.61)	.117
BP	10.0	113	569.9	2.97 (2.19-4.01)	<.001
2 components					
TG + HDL-C	1.5	8	215.7	1.29 (0.62-2.71)	.497
Waist + HDL-C	1.7	6	190.0	1.69 (0.72-3.98)	.230
TG + GLU	1.4	10	368.8	1.85 (0.94-3.62)	.073
Waist + TG	1.3	9	344.8	1.90 (0.94-3.84)	.075
TG + BP	2.1	19	427.3	1.99 (1.18-3.37)	.010
Waist + GLU	2.1	15	355.3	2.15 (1.22-3.80)	.009
GLU + HDL-C	1.7	12	342.7	2.82 (1.51-5.26)	.001
Waist + BP	4.9	62	630.4	3.44 (2.42-4.89)	<.001
BP + GLU	4.0	69	788.6	3.83 (2.71-5.42)	<.001
BP + HDL-C	2.4	56	1010.7	6.36 (4.43-9.14)	<.001
3 components					
Waist + TG + HDL-C	0.9	3	151.0	0.98 (0.31-3.16)	.975
Waist + TG + GLU	0.7	5	353.0	1.70 (0.68-4.27)	.260
TG + GLU + HDL-C	0.6	4	307.9	1.76 (0.64-4.84)	.273
Waist + GLU + HDL-C	0.8	4	258.8	1.85 (0.66-5.22)	.244
BP + GLU + HDL-C	1.0	10	467.6	2.38 (1.21-4.66)	.012
TG + BP + GLU	1.1	20	826.2	3.51 (2.07-5.93)	<.001
TG + BP + HDL-C	0.9	13	646.7	3.56 (1.96-6.49)	<.001
Waist + TG + BP	1.8	30	875.4	4.21 (2.68-6.60)	<.001
Waist + BP + GLU	2.7	53	961.4	5.14 (3.53-7.49)	<.001
Waist + BP + HDL-C	2.0	42	1003.7	6.20 (4.03-9.51)	<.001
4 or 5 components					
TG + BP + GLU + HDL-C	0.5	4	427.7	1.87 (0.67-5.20)	.230
Waist + TG + GLU + HDL-C	0.5	5	463.0	2.86 (1.13-7.23)	.027
Waist + TG + BP + GLU	1.4	24	847.2	4.02 (2.47-6.56)	<.001
Waist + BP + GLU + HDL-C	1.0	19	840.7	4.62 (2.67-7.99)	<.001
Waist + TG + BP + HDL-C	1.2	23	926.2	4.74 (2.86-7.85)	<.001
Waist + TG + BP + GLU + HDL-C	1.0	25	1260.7	6.67 (4.11-10.84)	<.001

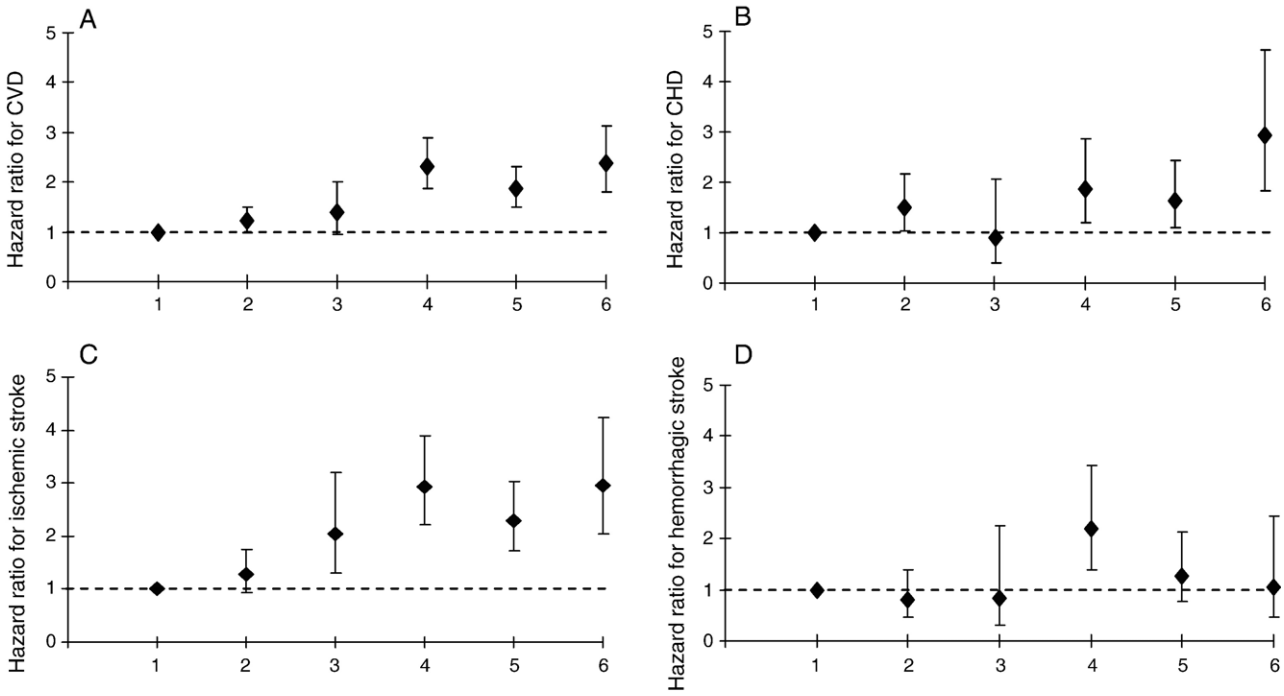
Waist, waist circumference ≥90 cm in men and ≥80 cm in women; TG, ≥150 mg/dL; BP, systolic BP ≥130 mm Hg and/or diastolic BP ≥ 85 mm Hg or on antihypertensive medication; GLU, ≥100 mg/dL or previously diagnosed diabetes; HDL-C, <40 mg/dL in men and <50 mg/dL in women.

As shown in Table II, IFG or diabetes were associated with higher incidence risk of CHD, ischemic stroke, and total CVD but not hemorrhagic stroke, compared with NFG. Subjects with MetS had higher risk of CHD, ischemic stroke, hemorrhagic stroke, and total CVD than those without MetS. The impact of MetS on CVD was further assessed according to the number of components and different combinations of the components. The latter was undertaken for total CVD only because the number of cases was limited for separate analysis of CHD and stroke. Cardiovascular disease risk increased in proportion to the number MetS components (Table II), and there was a wide variation depending on the profile of concomitant disorders. If only 1 component was present, elevated BP was the only significant predictor of CVD. The impact of hyperglycemia was slight and nonsignificant if no other components were coexisted. When 2 components were present, 6 of the 10 combinations were associated with significantly higher risk. However, all combinations of ≥3 components (MetS) had significant contribution, except for those rare phenotypes (<1% of the whole sample) (Table III).

To compare MetS with prediabetes and diabetes, the CVD risk was presented in Figure 2 according to presence or absence of MetS and glycemic status after adjusting nonmetabolic risk factors. In the absence of MetS, IFG and diabetes carried a mild and lower risk of developing CHD than MetS without IFG or diabetes, and the risk associated with IFG was higher than that for diabetes. When all forms of dysglycemia combined, hyperglycemia without MetS was associated with a mild and nonsignificant increased risk for CHD (HR 1.38, 95% CI 0.98-1.95), whereas MetS carried a significant risk of CHD even in the absence of hyperglycemia (HR 1.86, 95% CI 1.21-2.86), compared with subjects without either MetS or hyperglycemia.

Subjects with MetS had a higher incidence risk of ischemic stroke regardless of the level of dysglycemia

Figure 2



Hazard ratio and 95% CI for cardiovascular diseases associated with the MetS and dysglycemia after adjusting for age, sex, smoking, family history of CVD, and hypercholesterolemia by Cox proportional hazards model. X axis: 1/NFG without MetS (reference), 2/IFG without MetS; 3/diabetes without MetS, 4/NFG with MetS, 5/IFG with MetS; 6/diabetes with MetS.

(Figure 2). Nonetheless, even in the absence of MetS, diabetes was accompanied by a higher incidence of ischemic stroke, compared with those with either NFG or IFG. This was true even if those with isolated hyperglycemia did not have higher prevalence of elevated BP than those without hyperglycemia (Table I). Once MetS was present, the incidence of ischemic stroke rose markedly.

Of interest, neither IFG nor diabetes was accompanied by an increased risk of hemorrhagic stroke. Individuals with MetS had a higher risk of hemorrhagic stroke than did those without MetS (Table II). The significance of impact of MetS on hemorrhagic stroke, however, was lost for dysglycemic subjects when the data were controlled for non-MetS risk factors (Figure 2).

Discussion

The MetS consists of a clustering of metabolic risk factors and is associated with increased risk for CVD. One of the features of MetS is impaired glucose regulation. Several reports further indicate that dysglycemia, regardless of its severity, is accompanied by increased risk for CVD.[16-18] To date, the relative contributions of MetS and dysglycemia on CVD risk have not been dissected. For example, Alexander et al[6] indicated that most of the risk for CHD associated with diabetes in the US population, which is predominantly white, can be explained by the coexistence of the MetS. Howard et al[19] reported that the elevated CHD risk in diabetes largely depends on concomitant risk factors in American Indians. In contrast, Stern et al[20] reported that, in patients with existing CVD from the San Antonio Heart Study, which is predominantly Hispanic, most of CVD mortality occurs in persons with diabetes, whereas MetS independent of diabetes has little impact on mortality. To our knowledge, whether MetS carries any additional CVD risk after excluding both prediabetes and diabetes and whether hyperglycemia in prediabetes or diabetes carries any additional CVD risk independent of other metabolic disorders are yet to be defined. The current study was carried out in an effort to dissect the relative contributions of MetS and dysglycemia (including prediabetes and diabetes) to several forms of CVD in the Chinese population.

The overlap between MetS and dysglycemia in the Chinese population was marked. Sixty-two percent of persons with MetS had either IFG or diabetes. This overlap most likely can be attributed to a high prevalence of abdominal obesity in persons with MetS.

In addition, dysglycemia is one of the components of the MetS diagnosis, which added to the overlap. But an important question is whether the increased CVD risk that is associated with MetS and with dysglycemia can be explained by dysglycemia per se or whether the greater risk can be attributed to a clustering of metabolic risk factors.

Our study showed that in the Chinese population, the risk of developing CVD events in individuals with IFG or diabetes without MetS was mild and lower than the risk in those with MetS without IFG or diabetes. Isolated hyperglycemic did not manifest a significantly higher risk of developing CVD, unless other metabolic disorders were coexisted. These findings strongly suggest that the risk of CVD seen in those with IFG or diabetes was largely attributable to the accompanying multiple metabolic abnormalities rather than hyperglycemia per se. Our data are consistent with the findings from clinical trails, which indicated multifactorial intervention rather than only intensive glycemic control is better in reducing CVD risk in patients with diabetes.[21,22] These results point to the need to identify the clustering of metabolic aberrations accompanying the MetS. Detecting only diabetes or prediabetes is not sufficient to identify persons at higher risk for CVD because of metabolic disorders. Actually, about 40% of people with MetS did not manifest hyperglycemia. However, this group classified more people with obesity and other metabolic abnormalities, and their CVD risk had already increased significantly. Similarly, most patients with dyslipidemia (65.6% for high TG and 69.1% for low HDL-C) did not present hyperglycemia: they were either isolated dyslipidemia or clustered with obesity or hypertension. The high prevalence of isolated high TG or low HDL-C may partly be due to the high consumption of dietary carbohydrates in Chinese population.[23] Therefore, when data were split by the status of MetS, hyperglycemia was not associated with a higher prevalence of dyslipidemia.

Among the metabolic risk factors, hypertension has been reported to be the foremost contributor to risk for CVD in China.[2,24] In the present study, elevated BP was the only component of MetS, which carried significant CVD risk in absence of other disorders. A higher prevalence of hypertension was particularly evident in subjects with the MetS. This higher BP thus appears to be a prominent component of the MetS in China.[15] Although there is much focus on the MetS as a prediabetic condition and on concern about its association with a rising prevalence of diabetes in China, the importance of elevated BP as a cardiovascular risk factor in patients with the MetS and diabetes should not be overlooked.[25] Identification and early intervention of MetS is helpful to control hypertension and associated cardiovascular risk.

Another feature of the MetS in China was a much higher non–HDL-C level. It can be explained by elevated concentrations of both low-density lipoprotein cholesterol and very low-density lipoprotein cholesterol—markers for atherogenic apoB-containing lipoproteins.[26] An elevation of the latter lipoproteins must be recognized as an integral part of MetS in China and a significant contributor to CHD and stroke.[27,28]

Since most persons with MetS had dysglycemia, we can return to the question of whether most of the CVD risk associated with the MetS can be explained by an increase in plasma glucose levels. The data are consistent with some contribution of dysglycemia to CVD risk but, certainly, not all. Subjects with MetS and diabetes had higher rates of both CHD and ischemic stroke than did MetS subjects without diabetes. This suggests that the hyperglycemia of diabetes carries independent risk. The relatively low CHD risk associated with diabetes in the absence of MetS might be due to the limited cases in this group, given the fact that few people had diabetes but without MetS.

The contribution of different MetS traits to the incidence of CVD was also considered in the present study. Our results are concordant with the findings from the Framingham Heart Study[29] that the associated CVD risk for various number and combinations of MetS components was heterogeneous. Unlike their analysis which used the group without a specific combination as the comparator, we used the group without any component as the reference to explore the "net" effect of a specific trait. In the present study, all those with ≥ 3 components had significantly higher CVD risk, except for the rare combinations. Our data corroborate the rationale of defining the cluster of ≥ 3 disorders as MetS. Nevertheless, the specific contribution of various MetS traits to CHD and stroke needs to be investigated in future studies with more events.

This study provides strong evidence that the multiple metabolic risk factors accompanying MetS is a major cause of both CHD and stroke in China. Although there is a large overlap between MetS and dysglycemia in China, the association between MetS and CVD cannot be explained entirely by dysglycemia. Both hypertension and dyslipidemia, which are common in persons with the MetS, likely play an equal or greater role in the causation of CVD. The data are consistent with the concept that the Chinese population is susceptible to development of multiple cardiovascular risk factors with the onset of obesity.[3,30] If this is confirmed in further studies, it provides a strong rationale for early intervention in the public health sphere to prevent the epidemic of obesity that is occurring in several other countries.

References

1. Truelsen T, Mahonen M, Tolonen H, et al. Trends in stroke and coronary heart disease in the WHO MONICA Project. Stroke 2003;34:1346-52.

2. He J, Gu D, Wu X, et al. Major causes of death among men and women in China. N Engl J Med 2005;353:1124-34.
3. Wang Y, Mi J, Shan XY, et al. Is China facing an obesity epidemic and the consequences? The trends in obesity and chronic disease in China. Int J Obes (Lond) 2007;31:177-88.
4. Grundy SM, Cleeman JI, Daniels SR, et al. Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute scientific statement. Circulation 2005;112:2735-52.
5. Kahn R, Buse J, Ferrannini E, et al. The metabolic syndrome: time for a critical appraisal: joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2005;28:2289-304.
6. Alexander CM, Landsman PB, Teutsch SM, et al. NCEP-defined metabolic syndrome, diabetes, and prevalence of coronary heart disease among NHANES III participants age 50 years and older. Diabetes 2003;52:1210-4.
7. McNeill AM, Rosamond WD, Girman CJ, et al. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the atherosclerosis risk in communities study. Diabetes Care 2005;28:385-90.
8. Malik S, Wong ND, Franklin SS, et al. Impact of the metabolic syndrome on mortality from coronary heart disease, cardiovascular disease, and all causes in United States adults. Circulation 2004;110:1245-50.
9. Liu J, Hong Y, D'Agostino Sr RB, et al. Predictive value for the Chinese population of the Framingham CHD risk assessment tool compared with the Chinese Multi-Provincial Cohort Study. JAMA 2004;291:2591-9.
10. Wu Z, Yao C, Zhao D, et al. A prospective cohort study on cardiovascular disease incidence in 11 provinces of China, I: associations between risk factor level and cardiovascular disease incidence. Chin J Cardiol 1999;27:5-8.
11. MONICA Manual, Part IV: event Registration. (Accessed May 8, 2006, at http://www.ktl.fi/publications/monica/manual/part4/iv-1.htm).
12. Wu Z, Yao C, Zhao D, et al. Sino-MONICA project: a collaborative study on trends and determinants in cardiovascular diseases in China. Part I: morbidity and mortality monitoring. Circulation 2001;103:462-8.
13. Gutzwiller F. Monitoring of cardiovascular disease and risk factor trends: experiences from the WHO/MONICA project. Ann Med 1994;26:61-5.
14. Genuth S, Alberti KG, Bennett P, et al. Follow-up report on the diagnosis of diabetes mellitus. Diabetes Care 2003;26:3160-7.
15. Liu J, Grundy SM, Wang W, et al. Ethnic-specific criteria for the metabolic syndrome: evidence from China. Diabetes Care 2006;29:1414-6.
16. Meigs JB, Nathan DM, D'Agostino Sr RB, et al. Fasting and postchallenge glycemia and cardiovascular disease risk: the Framingham Offspring Study. Diabetes Care 2002;25:1845-50.
17. Wei M, Gaskill SP, Haffner SM, et al. Effects of diabetes and level of glycemia on all-cause and cardiovascular mortality. The San Antonio Heart Study. Diabetes Care 1998;21:1167-72.
18. Hu FB, Stampfer MJ, Solomon CG, et al. The impact of diabetes mellitus on mortality from all causes and coronary heart disease in women: 20 years of follow-up. Arch Intern Med 2001;161:1717-23.
19. Howard BV, Best LG, Galloway JM, et al. Coronary heart disease risk equivalence in diabetes depends on concomitant risk factors. Diabetes Care 2006;29:391-7.
20. Stern MP, Williams K, Hunt KJ. Impact of diabetes/metabolic syndrome in patients with established cardiovascular disease. Atheroscler Suppl 2005;6:3-6.
21. UK Prospective Diabetes Study (UKPDS) Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). Lancet 1998;352:837-53.
22. Gaede P, Vedel P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. N Engl J Med 2003;348:383-93.
23. Li L, Rao K, Kong L, et al. A description on the Chinese National Nutrition and Health Survey in 2002. Chin J Epidemiol 2005;26:478-84.
24. Wang W, Zhao D, Liu J, et al. A prospective study of relationship between blood pressure and 10-year cardiovascular risk in a Chinese cohort aged 35-64 years. Chin J Intern Med 2004;34:730-4.
25. Zhang Y, Lee ET, Devereux RB, et al. Prehypertension, diabetes, and cardiovascular disease risk in a population-based sample: the Strong Heart Study. Hypertension 2006;47:410-4.
26. Executive summary of the clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. Arch Intern Med 1998;158:1855-67.
27. Schulze MB, Shai I, Manson JE, et al. Joint role of non-HDL cholesterol and glycated haemoglobin in predicting future coronary heart disease events among women with type 2 diabetes. Diabetologia 2004;47:2129-36.
28. Athyros VG, Papageorgiou AA, Mercouris BR, et al. Treatment with atorvastatin to the National Cholesterol Educational Program goal versus 'usual' care in secondary coronary heart disease prevention. The GREek Atorvastatin and Coronary-heart-disease Evaluation (GREACE) study. Curr Med Res Opin 2002;18:220-8.
29. Wilson PW, D'Agostino RB, Parise H, et al. Metabolic syndrome as a precursor of cardiovascular disease and type 2 diabetes mellitus. Circulation 2005;112:3066-72.
30. Wildman RP, Gu D, Reynolds K, et al. Are waist circumference and body mass index independently associated with cardiovascular disease risk in Chinese adults? Am J Clin Nutr 2005;82:1195-202.