

Original Article

Continuous metabolic syndrome risk score for predicting cardiovascular disease in the Chinese population

Guo-Dong Kang MD¹, Lu Guo MD², Zhi-Rong Guo PhD³, Xiao-Shu Hu PhD⁴,
Ming Wu PhD¹, Hai-Tao Yang PhD¹

¹ Center for Diseases Control of Jiangsu Province, NanJing, Jiangsu, China

² Center for Diseases Control of Nanjing, Nanjing, Jiangsu, China

³ Department of Radiology & Public Health, Soochow University, Suzhou, Jiangsu, China

⁴ Health Bureau of Jiangsu Province, NanJing, Jiangsu, China

Although the metabolic syndrome (MetS) is a predictor of cardiovascular disease (CVD), the current dichotomous definition of MetS cannot be used to evaluate context-specific identification or for efforts to reduce the risk of CVD in the population. In this study, we assigned MetS a continuous risk score for predicting the development of CVD. In total, 3,598 participants recruited from the Jiangsu Province of China were followed for a median of 6.3 years. A total of 82 participants developed CVD during the follow-up period. Receiver operating characteristic (ROC) curve was used to analyze the association between components of MetS and CVD. The results show that systolic blood pressure (SBP) was associated with CVD more intimately (area under receiver-operator characteristic curve (AUC)=0.72, 95% confidence interval (CI), 0.66-0.77) than other features of MetS. When each MetS component was assigned according to the magnitude of regression coefficients in the Cox regression hazard model, the AUC of the continuous MetS risk score (AUC=0.80, 95% CI, 0.75-0.84) exceeded that of the dichotomized definition of MetS (AUC=0.63, 95% CI, 0.56-0.69) ($p<0.01$). The incidence of CVD increased with the MetS risk score. This prospective cohort study suggests that the use of continuous MetS risk score would significantly improve the capability for predicting the development of CVD compared to current definition of MetS. Further, the appropriate cut-off points need to be verified in other races and regions.

Key Words: the metabolic syndrome, cardiovascular disease, risk factors, prospective study, receiver operating characteristic curve

INTRODUCTION

Cardiovascular disease (CVD) is a leading cause of mortality and morbidity in developed and developing countries.^{1,2} The metabolic syndrome (MetS), initially described in 1988 by Reaven, is an important risk factor for CVD.³ For individuals diagnosed with MetS, the risk of developing CVD increases two- to five-fold compared to those without MetS.^{4,6} As defined by National Cholesterol Education Program Adult Treatment Panel III report (NECP ATP III),⁷ MetS is diagnosed when at least 3 of its 5 components are present. The components include greater waist circumference (WC), dyslipidemia with high triglycerides (TG), low high-density lipoprotein cholesterol (HDL-C) levels, elevated blood pressure (BP) and impaired fasting plasma glucose (IFPG).

Until now, various definitions relying on dichotomized cut-off points have been utilized to diagnose MetS.⁷⁻⁹ As the understanding of MetS has increased recently, controversies about the current definition of MetS have persisted.¹⁰⁻¹² The latest report of World Health Organization (WHO) suggested that MetS be considered a pre-morbid condition for predicting the development of CVD and type 2 diabetes (T2DM) rather than a clinical diagnosis.¹³

However, the current definition of MetS has limited practical utility as an evaluative or managerial tool. It is necessary to re-assess MetS so that it can be used to evaluate context-specific identification and reduce the risk of CVD and T2DM at the population level.

Meanwhile, it is well recognized that age is closely related to CVD risk factors,¹⁴ especially in older age groups, age plays the major role in the development of CVD.¹⁵ In fact, age is a confounding factor in the evaluation of the risk for CVD for participants with the same number of MetS components. Up to now, there is no definition of MetS that incorporates age. For this reason, age was taken into account alongside the MetS risk score in this study.

Therefore, the purpose of this study was to develop a continuous risk score model as an expanded understand-

Corresponding Author: Dr Zhirong Guo, Department of Radiology & Public Health, Soochow University. High Education Area, Industrial Park District, Suzhou 215123, China.
Tel: +86-512-65880079; Fax: +86-512-65884830
Email: guozhirong28@163.com

Manuscript received 5 November 2010. Initial review completed 23 June 2011. Revision accepted 22 August 2011.

ing of MetS and evaluate the performance of this continuous score for predicting the development of CVD in a Chinese population.

MATERIALS AND METHODS

Subjects

Baseline study

Participants were recruited from the Prevention of MetS and Multi-metabolic Disorders in Jiangsu Province of China Study (PMMJS). PMMJS is an ongoing prospective study. The aims of this study were to estimate the prevalence of MetS in the Jiangsu province of China at baseline and to evaluate the incidence of CVD and T2DM of participants at follow-up. This study was conducted in the Jiangsu province, which is located in the east part of China and has a population of 75 million, from early 2000 to 2004. The multi-stage sampling method was used at baseline survey; we randomly selected 3 sites from 13 urban districts and 9 sites from 52 counties of Jiangsu Province. Then, one community (similar to a street district or a residential committee) from each city and one rural township from each county were sampled randomly, respectively. Finally, individuals were randomly chosen from the selected communities and townships; only one participant was selected from each household, without replacement. All participants should possess the household registration in the local administrative institute. In all, 8,685 participants aged 35-74 years old were randomly selected at baseline from 12 primary units (each unit was about 1,000-2,000 households), stratified by age (10 years per group) and gender. There were 5,888 valid questionnaires at the end of baseline and the overall response rate was 92.0%. The investigation was supported by the local Centers for Diseases Control and Prevention (CDC). Participants were asked to go to the community health station with their clinical record or health registration card after giving informed consent. The protocol was approved by the ethical committee of Soochow University.

Detailed information collected included behavioral, lifestyle, demographic factors and body measurements. Weight and height were measured for all subjects. Body weight and height were measured to the nearest 0.1 kg and 0.1 cm, respectively. Sitting blood pressure was measured on the right arm by mercury sphygmomanometer, subjects were required to rest for at least 5 minutes before measurement, and were measured at 30 seconds intervals for three times. Both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were recorded, and the mean value of three measurements was recorded as the BP for analysis. Waist circumference was measured (at minimal respiration to the nearest 0.1 cm at the level of the iliac crest) twice to determine baseline WC for each subject. Blood sample was obtained after a minimum 8-hour fasting, the levels of FPG, TG and HDL-C were measured by the glucose oxidase enzymatic method, enzymatic method and precipitation method respectively. The measurements were conducted using an automatic biochemistry analyzer (Hitachi Inc, Tokyo Japan). All clinical and biological parameters were evaluated at the same day of the physical examination. Detailed information contained behavioral, lifestyle, demographic factors and measurements. Exclusions criteria for

the cohort were: pregnant women, people with severe cancer, disability and severe psychiatric disorders.

All subjects were given informed consent at the interview.

Follow-up study

During 2006 to 2008, participants recruited for this study who has reached at least five years were preceded a follow-up study. A total of 4,582 participants were followed. 4,083 subjects were included in the second investigation with a follow-up rate of 89.1%. The characteristics of individuals who did not attend follow-up survey, such as age, gender, and metabolic variables were similar to those included in the baseline study. Health status was checked by following health examinations, procedures at follow-up were similar with those at the baseline. The primary endpoints for follow-up survey were occurrence of CVD or T2DM. Subjects undergoing health examination or moving out from the original town were checked by mail or telephone. Also, we established a daily monitoring system among the study team, the chronic diseases surveillance and death registration at local CDC. For participants who reported their own health status, we asked them to provide their medical records. If the subject died during the period of follow up, an autopsy for determining cause of death was performed at the hospital where the subject died. In all, subjects with T2DM (n=289), CVD (n=36), body mass index <18.5 kg/m² (n=27), and missing data (n=133) at baseline were excluded from the study. Thus, up to July of 2008, 3,598 remaining subjects (1,451 men and 2,147 women) were enrolled into the follow-up study. The median of follow-up time was 6.3 person-years (range 5 to 8 years). The reliability and accuracy of collected data were checked for the study.

Definition of the metabolic syndrome

The definition of MetS used in this study is based on the revised National Cholesterol Education Program Adult Treatment Panel III (NECP-R ATP III) of 2005 for Asian populations.¹⁶ Based on this definition, the cut-off values for WC were 90 cm for men and 80 cm for women respectively, which were in accordance with modifications for Asian populations. The threshold of FPG was modified to 5.6 mmol/L, which could improve the prediction of diabetes in Asian populations. Elevated BP was defined as average SBP/DBP \geq 130/85 mmHg. Hypertriglyceridemia was defined as serum TG of \geq 1.7 mmol/L. Low HDL-C was defined as serum HDL-C level of <1.0 mmol/L in men or <1.3 mmol/L in women. MetS was defined as the presence of three or more of the components mentioned above.

Definition of cardiovascular diseases

Participants who met one of the following conditions were diagnosed as having CVD. Participants who experienced first-ever development of coronary heart disease (CHD) and stroke during the follow-up period were diagnosed with CVD. The criteria for a diagnosis of CHD included interventional therapy of the coronary artery (cardiac catheterization or coronary artery bypass grafting), stable angina pectoris, unstable angina pectoris, first occurrence of acute myocardial infarction, and congestive

heart failure caused by myocardial ischemia after baseline investigation. Stroke was classified as ischemic attack or hemorrhagic attack. Peripheral vascular disease (abdominal aneurysm, operation on vessels and carotid endarterectomy) was also included as CVD. The diagnosis of CVD and the determination of its pathological type were based on standard questionnaires, signs and symptoms in the clinical history, all available clinical data and autopsy findings. Cardiovascular death during follow-up was also defined as CVD (ICD-9 codes 390-459).

Statistical analysis

Continuous variables were tested using the t-test and non-parametric test. Frequencies of categorical variables were tested using the chi-square tests. The MetS risk score in this study was produced using the scoring system developed by Sullivan *et al.*¹⁷ In the MetS risk score model, points were assigned to each variable based on the magnitude of its regression coefficient in Cox proportional-hazards model. Scores associated with each category of each component were computed by the ratio of each regression coefficient to the constant for the score system. The constant was the number of regression units that reflect one point in the final risk score system, or the number of regression units that will correspond to one point. The constant in our study was set to be equivalent to the increase in risk associated with a 5-year increase in age. Each point was rounded to the nearest integer ratio. A total risk score for each individual was calculated by the sum of the points. This score system was related to actual observed incidence. Meanwhile, receiver operating characteristic (ROC) curve and calculation of the area under receiver operator characteristic curve (AUC) of the MetS risk score were performed. Sensitivity and specificity for each cut-off point were calculated. The cut-off point, which gave the maximum sum of sensitivity and specific-

ity, was taken as the optimum value.¹⁸

Because there were still no classification criteria for MetS components, we categorized variables based on the Framingham risk score (FRS) and other established guidelines. Classification of SBP, DBP and HDL-C were referenced to the FRS.⁷ TG were categorized by NCEP-ATPIII of 2005.¹⁶ For FPG, we consociated the diagnostic criteria of both the NCEP-ATPIII of 2005 and the Guidelines for the Prevention, Management and Care of Diabetes Mellitus proposed by WHO in 2006.^{16,19} Thus FPG was classified as <5.6, 5.6-6.1, 6.1-7.0 and ≥ 7.0 mmol/L, respectively. And WC was divided into quintiles according to men and women respectively. Age was stratified into quintiles. Analyses were performed with SPSS software version 13.0 and Medcalc software version 7.5.

RESULTS

A total of 82 participants had developed CVD during follow-up, there was no difference in incidence of CVD between men and women. Table 1 summarizes the general characteristics of the study population at baseline. Defined by NECP-R ATPIII, 25.5% of participants were diagnosed with MetS, women had higher prevalence of MetS than men. And the presence of 0, 1, 2, 3, 4 and 5 diagnostic components was observed in 19.5%, 30.9%, 24.1%, 16.0%, 7.1%, and 2.4% of participants, respectively. Hypertension was the most frequent individual contributor to the diagnosis of MetS (39.4% of participants) and WC was the least frequent contributor (23.8% of participants). Except for TG and FPG, women had higher prevalence of other features than men at baseline.

As shown in Table 2, when each component of MetS was analyzed by ROC curve with continuous variables, the AUC of each component for predicting the development of CVD was different. SBP, DBP, TG and HDL-C

Table 1. General Clinical and Biochemical Characteristics of the subjects at Baseline

Characteristics	Men	Women	p-value
n (Male)	1451	2147	-
Age (year)	50.6±9.8	50.0±19.0	NS
WC (cm)	77.6±9.2	76.0±9.2	<0.01
TG (mmol/L)	1.34 (0.92)	1.37 (0.88)	NS
SBP (mmol/L)	127±19.3	125±20.2	NS
DBP (mmHg)	81.5±11.2	78.8±10.5	<0.01
FPG (mmHg)	5.3±1.2	5.4±1.2	NS
HDL-C (mmol/L)	1.3±0.4	1.3±0.3	NS
WC (>90 cm of man, >80 cm of women) (%)	10.4	32.9	<0.01
TG (≥ 1.7 mmol/L) (%)	31.2	31.7	NS
SBP/DBP ($\geq 130/85$ mmHg) (%)	43.8	36.4	<0.01
FPG (5.6 mmol/L) (%)	24.2	26.3	NS
low HDL-C (<1.0 mmol/L of men, <1.3 mmol/L of women) (%)	29.4	59.4	<0.01
MetS (NECP-ATPIII) (%)	17.9	30.6	<0.01
CVD (%)	2.5	2.1	NS

Data are presented as mean \pm SD, percentage, or median value (interquartile range)

Abbreviations: WC, waist circumference; TG, triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; MetS, the metabolic syndrome; NECP-R ATPIII, Revised National Cholesterol Education Program Adult Treatment Panel III; CVD, Cardiovascular disease; NS, not significant.

Table 2. AUC of MetS and its components for predicting the development of CVD

Characteristics	AUC	95% CI	<i>p</i> value
WC	0.62	0.56-0.68	<0.01
TG	0.66	0.61-0.71	<0.01
SBP	0.72	0.66-0.77	<0.01
DBP	0.66	0.59-0.72	<0.01
FPG	0.55	0.48-0.62	NS
Low HDL-C	0.58	0.52-0.65	<0.05
MetS (NECP-R ATPIII)	0.63	0.56-0.69	<0.01

Abbreviation: AUC, area under receiver characteristic operating curve; CI, confidence interval; WC, waist circumference; TG, triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; MetS, the metabolic syndrome; NECP-R ATPIII, Revised National Cholesterol Education Program Adult Treatment Panel III; CVD, cardiovascular disease; NS, not significant.

Table 3. Pairwise comparison of ROC curves among MetS and its components (*p*-values)

Characteristics	WC	TG	SBP	DBP	FPG	Low HDL-C
WC	-					
TG	NS	-				
SBP	<0.05	NS	-			
DBP	NS	NS	<0.05	-		
FPG	NS	NS	<0.01	<0.05	-	
Low HDL-C	NS	NS	<0.01	NS	NS	-
MetS (NECP ATPIII)	NS	NS	<0.05	NS	<0.05	NS

Abbreviations: ROC, receiver operating characteristic; WC, waist circumference; TG, triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; MetS, the metabolic syndrome; NECP-R ATPIII, Revised National Cholesterol Education Program Adult Treatment Panel III; NS, not significant.

Table 4. Points of the metabolic syndrome risk score computed by Cox regression hazard model

Characteristics	Category of variables	RR (95% CI)	Regression coefficient	Points
Age (years)	Q1 (30.0-40.9)	ref	ref	0
	Q2 (41.0-45.9)	2.1 (0.2-23.7)	0.8	3
	Q3 (46.0-51.9)	10.6 (1.4-81.5)	2.4	9
	Q4 (52.0-58.9)	26.6 (3.6-195)	3.3	12
	Q5 (59.0-74.0)	34.3 (4.7-250)	3.5	13
WC (cm) (men/ women)	Q1 (55.0-69.6/ 50.0-67.9)	ref	ref	0/0
	Q2 (69.7-74.3/ 68.0-72.9)	3.0 (0.6-14.9)/ 1.2 (0.4-3.5)	1.1/0.2	3/1
	Q3 (74.4-79.9/ 73.0-77.5)	3.1 (0.6-15.2)/ 1.5 (0.5-4.2)	1.1/0.4	3/1
	Q4 (80.0-85.9/ 77.6-83.9)	5.1 (1.1-23.4)/ 1.8 (0.6-4.8)	1.6/0.6	5/2
	Q5 (86.0-115/ 84.0-115)	6.1 (1.4-27.2)/ 2.5 (1.0-6.6)	1.8/0.9	5/3
TG (mmol/L)	<1.7	ref	ref	0
	1.7-2.3	2.2 (1.3-3.8)	0.8	2
	2.3-5.7	2.0 (1.1-3.6)	0.7	2
	≥5.7	4.6 (1.8-11.7)	1.5	5
BP (mmHg)	SBP<120 and DBP<80	0.6 (0.3-1.1)	-0.5	-2
	SBP 120-129 or DBP 80-84	ref	ref	0
	SBP 130-139 or DBP 85-89	1.7 (0.9-3.2)	0.5	2
	SBP 140-159 or DBP 90-99	2.1 (1.2-3.9)	0.8	2
	SBP ≥160 or DBP ≥ 100	3.9 (1.9-8.1)	1.4	4
FPG (mmol/L)	<5.6	ref	ref	0
	5.6-6.1	1.2 (0.6-2.3)	0.2	1
	6.1-7.0	1.1 (0.3-2.2)	0.1	0
	≥7.0	3.9 (2.1-7.1)	1.4	4
HDL-C (mmol/L)	<1.0	1.6 (0.9-2.8)	0.5	2
	1.0-1.3	ref	ref	0
	1.3-1.5	1.4 (0.8-2.6)	0.4	1
	≥1.6	0.7 (0.3-1.5)	-0.4	-1

Abbreviations: RR, relative risk; ref, reference; Q, quintile; BP, blood pressure; ; WC, waist circumference; TG, triglyceride; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; FPG, fasting plasma glucose; MetS, the metabolic syndrome; NECP-R ATPIII, Revised National Cholesterol Education Program Adult Treatment Panel III; NS, not significant.

were associated with CVD, but FPG was no longer significantly associated with CVD. Pairwise comparison result indicates that the AUC of SBP was significantly of AUC among components of MetS were performed, the different with every other components of MetS, whereas the difference of AUC between other components were less significant. (Table 3)

Table 4 shows the classification standard and risk score for each categorized component of MetS in Cox proportional-hazards model. Scores were assigned based on the ratio of each component's regression coefficient to the constant for the score system. The values of scores correspond to the severity of MetS' components. The follow-

ing example illustrates the process used to determine the MetS risk score. Consider a participant with the following characteristics at baseline survey: male, 60 years old, WC 82.2 cm, TG 1.2 mmol/L, SBP/DBP 171/111 mmHg, FPG 8.2 mmol/L, HDL-C 1.3 mmol/L. The MetS risk score of this participant was calculated by the sum of scores of each categorized component: risk score points = Age (13) + WC (5) + TG (0) + SBP/DBP (4) + FPG (4) + low HDL-C (1) = 27. As a result, the total MetS risk score of the subjects ranged from -3 to 30. It should be mentioned that, during follow-up of the study, no participant was examined to express the highest values of each component of MetS at the same time. Therefore, no par-

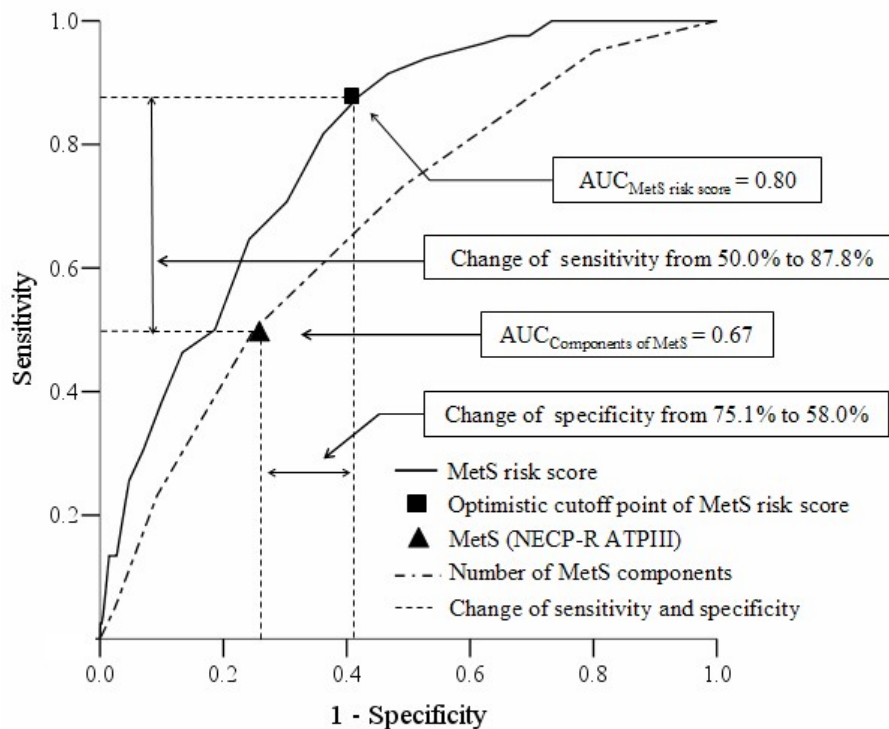


Figure 1. Comparison of continuous MetS risk score and the No. of MetS' components defined by NECP-R ATPIII for predicting the development of CVD. Abbreviations: AUC, area under receiver characteristic operating curve; MetS, the metabolic syndrome; NECP-R ATPIII, Revised National Cholesterol Education Program Adult Treatment Panel III

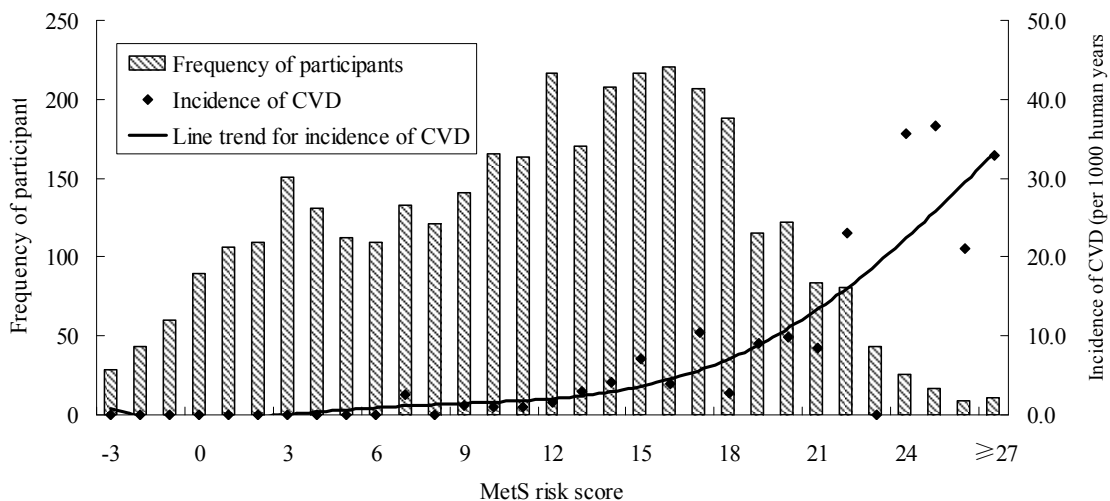


Figure 2. Incidence of CVD and its line trend according to the distribution of continuous MetS risk score. Abbreviations: CVD: cardiovascular disease; MetS, the metabolic syndrome.

participant had the highest scores of 33 for men and 31 for women respectively.

Figure 1 shows the ROC curve for the MetS risk score and the number of MetS' components (0-5) defined by NCEP-R ATP III. The maximum sum of sensitivity and specificity of the MetS risk score was taken as the optimum cut-off value. Consequently, a score of 13 was the optimum (sensitivity and specificity was 87.8% and 58.0%, respectively). However, the sensitivity and specificity of MetS as defined by NCEP-R ATP III were 50.0% and 75.1% respectively. Thus, the Youden's index of optimum MetS risk score was higher than the binary MetS. Additionally, the AUC of the MetS risk score was 0.80 (95% CI, 0.75 - 0.84), which exceeded that of the number of MetS' components (AUC=0.67, 95% CI, 0.62 - 0.73) significantly ($p<0.01$).

The incidence of CVD and its linear trend according to the distribution of MetS risk scores is shown in Figure 2. MetS risk scores in our study population were distributed on a nearly normal curve, and the risk of developing CVD increased with the MetS risk score. Most subjects had a low to intermediate-low risk of developing CVD; only those subjects whose score were in the upper quartile have high risk of developing CVD.

DISCUSSION

In our study, the AUC of MetS as defined by NCEP-R ATP III did not exceed that of the components itself, and the AUC of SBP was higher than other components. There were some controversies regarding whether MetS can provide more predictive information for the onset of CVD, independent of its individual components.^{20,21} Our previous study²² and other studies^{23,24} took into consideration that BP has a greater impact on the development of CVD than other components of MetS. In contrast, FPG was no longer significant for predicting CVD in our study. This lack of association may be because there are many theoretical pathways such as prothrombotic states, inflammation factors, lipoprotein metabolism, physical activity and drug therapy that can mediate the association between FPG and CVD. Similarly, studies of non-diabetic glycemia in Korean men²⁵ and British women²⁶ have shown no association between FPG and CHD. Also, a 15-year follow-up cohort study in western Scotland indicated that elevated FPG is not associated with long-term risk of CVD events in men.²⁷ And only a weak association between impaired fasting glycemia and CVD was found in another study of the Chinese population.²⁸ Thus, various combinations components of MetS may have different contributions to increased risk of CVD.

Although many studies have addressed the usefulness of MetS in identifying CVD risk, most of these studies were carried in the field of epidemiology in the last decade, and dichotomized cut-off points were used to diagnose MetS. The aim of the original concept for MetS itself was to encourage individuals who were diagnosed as MetS to pay attention to the clustering of often overlooked cardiovascular risk factors with the aim of improving cardiovascular prevention strategies; it was not intended for conducting clinical diagnosis.^{13,29} However, the dichotomized definition cannot evaluate the risk of patients with different combinations of components. Cut-

off values for the components of MetS implied that values above the specified thresholds were associated with excess risk. The rationale for the specific cut-off points, as opposed to higher or lower values, has never been delineated. Such dichotomized definitions mainly rely on relative risk (RR) or odds ratios (ORs) to assess the significance of the risks. Cut-off values of MetS are likely to perform less well when applied to populations where the mean levels of the risk factors differ from those population in which the cut-off points were initially developed.^{30,31} Until now, there was no evidence indicating that current definition of MetS can improve our ability to identify 'actual' CVD risk for individuals.

Furthermore, the current dichotomized definition had another potential shortcoming. Those participants whose biological or measurement test values were on the borderline of definition were difficult to classify. For example, a very minor improvement of one variable could result in an individual no longer qualifying for a MetS designation. This issue is so important that it cannot be neglected. A certain number of participants in our cohort initially diagnosed as having MetS were re-diagnosed as 'normal' by the dichotomized criteria after follow-up, only because of minimal changes in measures. In other words, it is uncertain that an individual with a cluster of three components has substantially increased risk of CVD over an individual with only two components.¹¹

The method of assigning MetS with a continuous score rather than a dichotomous definition can avoid these deficiencies. Because the degree of risk for the development of CVD can be evaluated by the level of the score, a modest change in only one variable will result in only a modest change in the overall MetS score. Our results show that the ability to predict CVD was clearly promoted when MetS components were weighted in assignment to become a continuous risk score. Meanwhile, for those participants who had 1 or 2 abnormal components, and thus were not diagnosed with MetS, the level of a continuous score can help estimate the severity of CVD risk.

The incidence of CVD increased with MetS risk score, especially for participants who were in the upper quartile of scores. This phenomenon reveals that MetS has successive risk for the development of CVD and the risk of MetS developing CVD is not in a linear trend. A recent report of WHO indicated that MetS should not be applied as a clinical diagnosis and should instead be used for developing and evaluating population-based prevention measures.¹³ The performance of the MetS risk score may promote an understanding of MetS that returns it to its original educational intent. In short, a continuous risk score may be beneficial for public health strategies. Physicians can identify the degree of CVD risk and provide different health interventions according to the distribution of scores to the public.³²

The relative predictive ability for predicting CVD of the MetS risk score compared to the FRS should be noted. Some studies suggested that MetS was inferior to the FRS for predicting CVD.^{33,34} Making a CVD risk assessment, using dichotomous variables leads to the loss of crucial information concerning the magnitude of the risk factors.³⁵ Our study demonstrates that when MetS is as-

signed into continuous risk score, the sensitivity and specificity of the optimum point improve significantly. The purpose of this study is not to develop a new 'FRS'. However, a continuous risk score derived from the components of the current MetS definition can be used as a tool for early-life determination of metabolic risk. Because some CVD risk factors such as obesity and FPG are not included in the FRS, the FRS and the MetS risk score could be used as two distinct tools in efforts to predict the development of CVD

The limitations of our study need to be pointed out. First, because data on subjects who had developed CVD were collected from medical records or health registration cards, patients who developed CVD without symptoms may have been excluded. The influence of these subclinical CVD patients on the MetS risk score was not analyzed in this study. Second, the threshold values of components came from published guidelines or statistics methods. The appropriate cut-off points for MetS need to be verified in prospective cohort studies with long-term follow-up and large study samples in the future. And the performance of a continuous MetS risk score in other races and regions should be validated.

In conclusion, the results of this study imply that the usefulness of continuous MetS risk score for predicting CVD exceeds that of the current dichotomized definition. The performance of the MetS risk score may promote an understanding of MetS closer to its original educational intent for public health. Moreover, more research are called for in the future to determine reasonable cut-off values for MetS components and the effectiveness of continuous MetS risk score in other regions and races.

ACKNOWLEDGMENTS

This study was supported in part by the CDC of Jiangsu province, Nanjing, China and the local community health station.

FUNDING

This research was supported by the Scientific Research Fund WKJ2004-2-014 of Ministry of Public Health, China.

AUTHOR DISCLOSURES

All authors have approved the manuscript. There are no conflicts of interest to disclose.

REFERENCES

- Solymoss BC, Bourassa MG, Lesperance J, Levesque S, Marcil M, Varga S, Campeau L. Incidence and clinical characteristics of the metabolic syndrome in patients with coronary artery disease. *Coron Artery Dis*. 2003;14:207-12.
- Lopez-Jaramillo P, Casas JP, Bautista L, Serrano NC, Morillo CA. An integrated proposal to explain the epidemic of cardiovascular disease in a developing country. From socioeconomic factors to free radicals. *Cardiology*. 2001;96:1-6.
- Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. *Diabetes*. 1988;37:1595-607.
- Girman CJ, Rhodes T, Mercuri M, Pyorala K, Kjekshus J, Pedersen TR, Beere PA, Gotto AM, Clearfield M. The metabolic syndrome and risk of major coronary events in the Scandinavian Simvastatin Survival Study (4S) and the Air Force/Texas Coronary Atherosclerosis Prevention Study (AFCAPS/TexCAPS). *Am J Cardiol*. 2004;93:136-41.
- Hu G, Qiao Q, Tuomilehto J, Balkau B, Borch-Johnsen K, Pyorala K. Prevalence of the metabolic syndrome and its relation to all-cause and cardiovascular mortality in nondiabetic European men and women. *Arch Intern Med*. 2004;164:1066-76.
- He Y, Jiang B, Wang J, Feng K, Chang Q, Fan L, Li X, Hu FB. Prevalence of the metabolic syndrome and its relation to cardiovascular disease in an elderly Chinese population. *J Am Coll Cardiol*. 2006;47:1588-94.
- Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA*. 2001;285:2486-97.
- Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1. diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. *Diabet Med*. 1998;15:539-53.
- Alberti KG, Zimmet P, Shaw J. The metabolic syndrome--a new worldwide definition. *Lancet* 2005; 366:1059-62.
- Kahn R, Buse J, Ferrannini E, Stern M. The metabolic syndrome: time for a critical appraisal. Joint statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia*. 2005;48:1684-99.
- Kahn R. Metabolic syndrome: is it a syndrome? Does it matter? *Circulation*. 2007;115:1806-10.
- Giampaoli S, Stamler J, Donfrancesco C, Panico S, Vanuzzo D, Cesana G et al. The metabolic syndrome: a critical appraisal based on the CUORE epidemiologic study. *Prev Med*. 2009;48:525-31.
- Simmons RK, Alberti KG, Gale EA, Colagiuri S, Tuomilehto J, Qiao Q et al. The metabolic syndrome: useful concept or clinical tool? Report of a WHO Expert Consultation. *Diabetologia*. 2010;53:600-5.
- Kastelein J. Cardiovascular risk-through the ages. *Atheroscler Suppl*. 2004;5:1-2.
- Tuomilehto J. Impact of age on cardiovascular risk: implications for cardiovascular disease management. *Atheroscler Suppl*. 2004;5:9-17.
- Grundy SM, Cleeman JI, Daniels SR, Donato KA, Eckel RH, Franklin BA 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.
- Sullivan LM, Massaro JM, D'Agostino RB Sr. Presentation of multivariate data for clinical use: The Framingham Study risk score functions. *Stat Med*. 2004;23:1631-60.
- Zweig MH, Campbell G. Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. *Clin Chem*. 1993;39:561-77.
- World Health Organization. Guidelines for the prevention, management and care of diabetes mellitus. EMRO Technical publications series 32, Geneva: 2006. pp. 28-33.
- Oda E. The metabolic syndrome (emperor) wears no clothes: response to Kahn. *Diabetes Care*. 2006;29:2566.
- Ding EL, Smit LA, Hu FB. The metabolic syndrome as a cluster of risk factors: is the whole greater than the sum of its parts? comment on "The metabolic syndrome, its component risk factors, and progression of coronary atherosclerosis". *Arch Intern Med*. 2010;170:484-5.
- Kang G, Guo L, Guo Z, Hu X, Wu M, Zhou Z, Zhou H, Liu S, Chen F. Impact of blood pressure and other components of the metabolic syndrome on the development of cardiovascular disease. *Circ J*. 2010;74:456-61.
- Tseng CH, Chong CK, Tseng CP, Shau WY, Tai TY. Hypertension is the most important component of metabolic syndrome in the association with ischemic heart disease in

- Taiwanese type 2 diabetic patients. *Circ J*. 2008;72:1419-24.
24. Shin CY, Yun KE, Park HS. Blood pressure has a greater impact on cardiovascular mortality than other components of metabolic syndrome in Koreans. *Atherosclerosis*. 2009;205:614-9.
 25. Song HJ, Shim KN, Yoon SJ, Kim SE, Oh HJ, Ryu KH et al. The prevalence and clinical characteristics of reflux esophagitis in Koreans and its possible relation to metabolic syndrome. *J Korean Med Sci*. 2009;24:197-202.
 26. Lawlor DA, Fraser A, Ebrahim S, Smith GD. Independent associations of fasting insulin, glucose, and glycated haemoglobin with stroke and coronary heart disease in older women. *PLoS Med*. 2007;4:e263.
 27. Preiss D, Welsh P, Murray HM, Shepherd J, Packard C, Macfarlane P, Cobbe S, Ford I, Sattar N. Fasting plasma glucose in non-diabetic participants and the risk for incident cardiovascular events, diabetes, and mortality: results from WOSCOPS 15-year follow-up. *Eur Heart J*. 2010;31:1230-6.
 28. Liu J, Grundy SM, Wang W, Smith SC Jr, Vega GL, Wu Z, Zeng Z, Zhao D. Ten-year risk of cardiovascular incidence related to diabetes, prediabetes, and the metabolic syndrome. *Am Heart J*. 2007;153:552-8.
 29. Reaven GM. The metabolic syndrome: time to get off the merry-go-round? *J Intern Med*. 2011;269:127-36.
 30. Wang JJ, Li HB, Kinnunen L, Hu G, Jarvinen TM, Miettinen ME, Yuan S, Tuomilehto J. How well does the metabolic syndrome defined by five definitions predict incident diabetes and incident coronary heart disease in a Chinese population? *Atherosclerosis*. 2007;192:161-8.
 31. Sone H, Mizuno S, Fujii H, Yoshimura Y, Yamasaki Y, Ishibashi S et al. Is the diagnosis of metabolic syndrome useful for predicting cardiovascular disease in Asian diabetic patients? Analysis from the Japan Diabetes Complications Study. *Diabetes Care*. 2005;28:1463-71.
 32. Sattar N, Forouhi NG. Metabolic syndrome criteria: ready for clinical prime time or work in progress? *Eur Heart J*. 2005;26:1249-51.
 33. Stern MP, Williams K, Gonzalez-Villalpando C, Hunt KJ, Haffner SM. Does the metabolic syndrome improve identification of individuals at risk of type 2 diabetes and/or cardiovascular disease? *Diabetes Care*. 2004;27:2676-81.
 34. McNeill AM, Rosamond WD, Girman CJ, Golden SH, Schmidt MI, East HE, Ballantyne CM, Heiss G. The metabolic syndrome and 11-year risk of incident cardiovascular disease in the atherosclerosis risk in communities study. *Diabetes Care*. 2005;28:385-90.
 35. Eddy DM, Schlessinger L, Heikes K. The metabolic syndrome and cardiovascular risk: implications for clinical practice. *Int J Obes (Lond)*. 2008;32:S5-10.

Original Article

Continuous metabolic syndrome risk score for predicting cardiovascular disease in the Chinese population

Guo-Dong Kang MD¹, Lu Guo MD², Zhi-Rong Guo PhD³, Xiao-Shu Hu PhD⁴, Ming Wu PhD¹, Hai-Tao Yang PhD¹

¹ Center for Diseases Control of Jiangsu Province, NanJing, Jiangsu, China

² Center for Diseases Control of Nanjing, Nanjing, Jiangsu, China

³ Department of Radiology & Public Health, Soochow University, Suzhou, Jiangsu, China

⁴ Health Bureau of Jiangsu Province, NanJing, Jiangsu, China

應用連續性代謝綜合征評分預測中國人群心血管疾病發病風險

儘管代謝綜合征(MetS)是心血管疾病(CVD)的一個預測因子，但目前代謝綜合征的二分法歸類無法用來評估心血管疾病特定風險或用於減小 CVD 發病的風險。在本研究中，賦予代謝綜合征連續性的風險評分，並應用來預測 CVD 的發病風險。共納入 3598 名來自中國江蘇省的研究對象，隨訪的中位年限為 6.3 年。隨訪期間共發生心血管疾病 82 例。利用接受者操作特徵曲線(ROC)來分析 MetS 與 CVD 的關係。結果顯示收縮壓(SBP)較其他組分與 CVD 的關係更為密切；曲線下面積(AUC)=0.72，95%可信區間：0.66-0.77。根據 COX 回歸風險模式的回歸係數對 MetS 各組分進行評分，結果連續性 MetS 評分的曲線下面積(AUC=0.80，95%可信區間：0.75-0.84)超過 MetS 二分法歸類的面積(AUC=0.63，95%可信區間：0.56-0.69)($p<0.01$)。CVD 發病率隨著 MetS 評分增加。本研究顯示，連續性 MetS 評分比起當前的 MetS 定義更有助於提高 CVD 發病風險的預測能力。代謝綜合征各組分合理的切點需要在其他人種和地區進一步證實。

關鍵字：代謝綜合征、心血管疾病、危險因素、前瞻性研究、接受者操作特徵曲線