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Including selective metabolic components in current diagnostic criteria does not improve discriminative validity for metabolic syndrome: a risk score approach

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Abstract

Objective: To examine whether including additional metabolic components to the current five-marker system can improve the discriminative validity for diagnosing metabolic syndrome (MetS).

Methods: This longitudinal cohort study included data from subjects that had completed at least three health examinations during a 5-year period. The study outcome was the onset of MetS. Sociodemographic and biochemical variables were recorded for all subjects so that the adjusted relative risks (ARRs) could be calculated for 11 metabolic components. Risk scores for the development of MetS based on the ARR values were determined. The sums of the risk scores of different component combinations were used to conduct a receiver operating characteristic (ROC) curve analysis of MetS diagnosis.

Results: A total of 3368 individuals with complete data was analysed. The ARRs of the 11 metabolic components were all statistically significant. According to ROC analysis, although good discriminative validity (area under the curve [AUC] range, 0.954–0.976) could be achieved for MetS diagnosis by using either all 11 or combinations of six metabolic components (the five current components plus one extra component), the current five metabolic components used for diagnosis had the best discriminative validity (AUC = 0.977).

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Conclusion: The current five metabolic components used for the diagnosis of MetS still represent the best combination with the highest discriminative validity.

Keywords
Metabolic syndrome, diagnostic criteria, risk score, receiver operating characteristic curve analysis

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Introduction

Diagnosis of the metabolic syndrome (MetS) by the current medical community usually adopts the standard of using the five markers suggested by the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III): waist circumference (waist), fasting glucose (FG), blood pressure, triglyceride (TG) and high-density lipoprotein cholesterol (HDL-C).[1] However, due to the rather complex mechanisms involved in the development of MetS,[2] increasing numbers of studies have suggested that other physical or biochemical factors that are closely associated with MetS should also be incorporated into the MetS diagnostic criteria. For example, MetS is closely associated with other chronic diseases such as cardiovascular disease (CVD) and type 2 diabetes mellitus, which in turn are linked to cholesterol and low-density lipoprotein cholesterol (LDL-C) levels, two important metabolic components.[3] In addition, for many patients, MetS takes the form of hepatic steatosis, a condition not only linked to TG levels but also to LDL-C levels.[4] These data demonstrate that cholesterol and LDL-C are also important for MetS diagnosis.[5]

Hepatic steatosis can also lead to abnormal liver function, so including two common liver function markers, namely glutamic-oxaloacetic transaminase (GOT) and glutamic-pyruvic transaminase (GPT), as diagnostic markers for MetS would appear to be a rational idea. In particular, raised GPT levels are regarded as a result of insulin resistance[6] and considered to be a better diagnostic marker for MetS than fasting blood glucose.[7]

Some researchers suggest that uric acid (UA) and/or hyperuricaemia should be considered as MetS markers[8,9] because epidemiology studies showed that hyperuricaemia acts as either a correlate[10–12] or an independent risk factor for MetS.[13,14] However, other studies have argued that hyperuricaemia is only a manifestation of CVD[15,16] and that the use of medications to lower UA levels does not prevent the development of CVD.[17] Therefore, the role of UA in MetS diagnosis remains to be clarified.

Recent studies have shown that in East Asian countries, body mass index (BMI) and waist circumference both have good discriminative ability for MetS,[18–20] yet there are insufficient solid data to refer to in order to tell which marker is better for predicting MetS. Therefore, the present study used large-scale community follow-up survey samples to perform a comprehensive analysis of the MetS predictability of a variety of biomarkers, especially focusing on blood lipid markers, liver function markers and uric acid. This present study also compared the discriminative ability of

waist circumference and BMI in predicting MetS, in the hope of offering references for future revisions to the MetS diagnostic criteria.

A risk score (RS)-based analysis was successfully applied to identify the factors used to predict type 2 diabetes mellitus,[21] but has never been used in MetS studies. Because the factors associated with MetS are more multivariate and complex than those for other CVD, using an RS-based analysis to identify potential predictors and combining the analysis with receiver operating characteristic (ROC) curve analysis can effectively enable identification of markers with higher discriminative validity and help identify the best combination for diagnosis.

Subjects and methods

Participants

Using multi-stage probability proportional to size sampling strategy, this longitudinal cohort study randomly invited residents who were ≥30 years of age with a registered household in Pingzhen District, Taoyuan City, Taiwan to undertake free health examinations in the Department of Community Medicine, Landseed Hospital, Tao-Yuan, Taiwan annually for 5 consecutive years between 2007 and 2011. These subjects were known as the 'Landseed Cohort'. For sample consistency and data integrity, only those who completed at least three health examinations in the 5-year period were included in the study. In addition, to understand the causality between metabolic components and MetS, subjects that were diagnosed with MetS at the first health examination were excluded from the study.

This study was approved by the Institutional Review Board of Landseed Hospital (no. LHIRB 15-003-B1). All subjects provided their written informed consent.

Measures

Metabolic syndrome. This study set the onset of MetS as the outcome. MetS was diagnosed according to the NCEP-ATP III criteria.[1] However, in light of the differences between ethnicity, Taiwan's National Health Agency engaged World Health Organization Expert Consultation in 2004[22] and proposed a revision of the waist standard, under which male and female waist circumferences needed to be ≥90 cm and ≥80 cm, respectively. The revised criteria were in line with those of International Diabetes Federation (IDF) recommended for Chinese ethnicity.[23] Nevertheless, unlike the IDF criteria making waist the central and essential component, a subject was defined as having MetS with the presence of three or more of the following five components in this study: (i) raised TG (≥110 mg/dl); (ii) reduced HDL-C (<40 mg/dl in males and < 50 mg/dl in females); (iii) raised blood pressure (systolic blood pressure [SBP] ≥130 mmHg or diastolic blood pressure [DBP] ≥85 mmHg); (iv) raised FG (≥100 mg/dl); (v) central obesity (waist circumference ≥90 cm in males and ≥80 cm in females).

Potential predictors of MetS. Each 'Landseed Cohort' subject underwent general physical examinations during the health examinations and blood and urine samples were collected for biochemical tests. A total of 31 markers were examined in this study. General examinations included height (cm), weight (kg), body fat (%), BMI (kg/m^2), waist circumference (cm), hip circumference (cm), SBP (mm/Hg), DBP (mm/Hg) and bone mineral density (BMD). Urine tests included total protein (g/dl) and pH value. Blood tests included white blood cell count (WBC, $10^6/mm^3$), red blood cell count (RBC, $10^6/mm^3$), platelet count (*1000/μl), haemoglobin (Hb, pg),

haematocrit (HCT, %), mean corpuscular haemoglobin (MCH, pg), mean corpuscular-haemoglobin concentration (MCHC, %) and mean corpuscular volume (MCV, fl). Biochemical tests included FG (mg/dl), albumin (g/dl), globulin (g/dl), blood urea nitrogen (BUN, mg/dl), creatinine (mg/dl), UA (mg/dl), cholesterol (mg/dl), TG (mg/dl), HD-C (mg/dl), LDL-C (mg/dl), GOT (IU/l) and GPT (IU/l). Among them, BMI, SBP, DBP, TG, HDL-C and FG were selected according to MetS definition.[1,23] The others were included based on previous studies such as BMD,[24] WBC,[25] Hb,[26] HCT,[27] UA,[8,9] LDL-C[4] and GPT.[6,7] As each subject had at least three health examinations, this study used the marker data from the first examination for this analysis.

Statistical analyses

All statistical analyses were performed using the SAS® statistical package, version 9.4 (SAS Institute, Cary, NC, USA) for Windows®. Sociodemographic characteristics between subject groups with and without MetS were compared using χ^2-test. To evaluate the effects of different markers on MetS, Student's *t*-test was applied to compare the differences in markers between subject groups with and without MetS. A P-value < 0.05 was considered statistically significant. Cohen's d was used to evaluate the effect size (ES). The metabolic components selected based on ES were then divided into two groups: 'normal' and 'abnormal', according to general clinical standards. Multiple Poisson regression was applied, with the basic demographic variables as the control variables to evaluate the adjusted relative risk (ARR) of each metabolic component for MetS. The risk score (RS) of each metabolic component was then calculated based on their ARR. The RS was defined as 2, 3, 4 or 5 when the ARR fell between 1 and 2, 2 and 4, 4 and 15, or was > 15, respectively.

To identify the best-fit model for predicting MetS using metabolic components, the present study proposed several potential combinations of metabolic components and retrieved the sum RS after summing the RSs of metabolic components in different combinations. The sum RS was then used to predict the future development of MetS. Model validation was performed using ROC curves and the applied area under the curve (AUC) was used as the indicator for model fitness, where a higher AUC indicated a better model.

Results

This longitudinal cohort study randomly selected 15 000 subjects aged $\geq$30 years from the 198 375 residents who registered their household in Pingzhen District, Taoyuan City, Taiwan and invited them for free health examinations annually for 5 consecutive years between 2007 and 2011. The 'Landseed Cohort' totalled 5757 individuals from the 15 000 invited subjects. For sample consistency and data integrity, only those who completed at least three health examinations in the 5-year period ($n = 3644$) were included in the study. In addition, to understand the causality between metabolic components and MetS, subjects who were diagnosed with MetS at the first health examination ($n = 276$) were excluded from the study. A total of 3368 subjects, with a mean age of 63.03 years for males and 59.21 years for females, were included in the follow-up analysis, of whom 409 developed MetS.

The 5-year cumulative incidence rate of MetS was 12.14% (409/3368) in the present study. Subjects with MetS were slightly older ($\chi^2 = 22.94$; $P < 0.001$), more highly educated ($\chi^2 = 28.04$; $P < 0.001$) and had a greater personal income ($\chi^2 = 9.99$; $P = 0.007$) than those without MetS

Table 1. Distribution of sociodemographic variables of the study sample ($n = 3368$) and their comparisons between subjects with and without metabolic syndrome.

				Metabolic syndrome					
		Total sample $n = 3368$		Yes $n = 409$		No $n = 2959$			
Variable		*n*	%	*n*	%	*n*	%	χ^2	Statistical significance
Age	<49	629	18.68	41	10.02	588	19.87	22.94	$P < 0.001$
	≥50	2739	81.32	368	89.98	2371	80.13		
Sex	Female	1898	56.35	202	49.39	1696	42.68	9.18	$P = 0.001$
	Male	1470	43.65	207	50.61	1263	57.32		
Educational level[a]	Low	1349	40.05	213	52.08	1136	38.39	28.04	$P < 0.001$
	High	2019	59.95	196	47.92	1823	61.61		
Marital status[b]	Married	2862	90.60	349	91.12	2513	90.53	0.14	NS
	Other	297	9.40	34	8.88	263	9.47		
Personal income, NTD[c]	<500 k	2765	84.02	354	88.50	2411	83.40	9.99	$P = 0.007$
	500 k–1 m	453	13.76	35	8.75	418	14.46		
	>1 m	73	2.22	11	2.75	62	2.14		

[a]Low educational level: having ≤ 9 years of education (up to around 15–16 years of age); high educational level: having > 9 years of education.
[b]Other includes not married, separated, divorced or widowed; 209 subjects did not provide information on marital status.
[c]New Taiwan Dollar; 1 NTD = 0.032 USD; 77 subjects did not provide information on personal income.
χ^2-test used to compare the two groups based on the presence of metabolic syndrome; NS, no significant between-group difference ($P \geq 0.05$).

(Table 1). Males were more likely to have MetS than females ($\chi^2 = 9.18$; $P = 0.001$), but marital status was not associated with the occurrence of MetS.

The differences in all physical and biochemical variables between the MetS group and the non-MetS group are shown in Table 2. Of the 31 biomarkers included in the comparison, a total of 10 items had a medium effect size (i.e. Cohen's d ≥0.5). Among them, as weight and BMI were highly related markers, only BMI, which had a higher effect size, was included in the following analysis, even though both markers had reached or surpassed a medium effect size. Similarly, although hip circumference had a medium effect size, it was strongly related to waist circumference, so only waist circumference was included in the subsequent analysis. To better evaluate the effects of blood lipid and hepatic inflammatory markers, the analysis included cholesterol, LDL-C, GOT and GPT in further analyses, even though the four markers failed to attain a medium effect size. A total of 11 potential metabolic components were selected for further analysis.

According to the multiple Poisson regression model, all selected 11 metabolic components had significant effects on MetS (Table 3). The risk of developing MetS for subjects with central obesity was 20-times (ARR 19.60; 95% confidence interval [CI] 15.24, 25.22) greater than that for normal controls. Cholesterol had the smallest effect size, for which subjects with a higher cholesterol level were 1.35-times (ARR 1.35; 95% CI 1.13, 1.62) more likely to develop MetS than the normal controls. To balance the weights of each metabolic component,

Table 2. Distribution of physical and biochemical markers between subjects with and without metabolic syndrome.

	Total sample $n=3368$		Metabolic syndrome: Yes $n=409$		Metabolic syndrome: No $n=2959$				
Biomarkers	Mean	SD	Mean	SD	Mean	SD	t	Statistical significance	ES (d)
Fasting glucose, mg/dl	91.89	23.48	108.50	37.43	89.61	19.80	9.92	$P<0.0001$	0.51
Creatinine, mg/dl	0.97	0.39	1.05	0.40	0.96	0.39	4.61	$P<0.0001$	0.24
Cholesterol, mg/dl	200.37	35.86	206.10	39.48	199.60	35.27	3.16	$P=0.0017$	0.16
Triglyceride, mg/dl	126.22	108.53	231.10	183.30	111.70	83.90	12.99	$P<0.0001$	0.65
High-density lipoprotein-cholesterol, mg/dl	60.23	15.36	46.56	10.92	62.12	14.92	–25.69	$P<0.0001$	–1.42
Low-density lipoprotein-cholesterol, mg/dl	124.79	32.37	128.50	34.34	124.30	32.06	2.45	$P=0.0143$	0.12
Systolicblood pressure, mm/Hg	123.57	19.13	136.50	18.81	120.30	17.79	15.87	$P<0.0001$	0.86
Diastolicblood pressure, mm/Hg	75.03	11.68	83.17	12.04	73.01	10.67	15.20	$P<0.0001$	0.84
Height, cm	159.44	8.09	158.90	8.15	159.50	8.08	–0.90	NS	–0.07
Weight, kg	61.19	15.78	67.09	11.42	60.65	16.02	6.21	$P<0.0001$	0.56
Body mass index, kg/m^2	24.01	5.96	26.49	3.36	23.79	6.10	8.45	$P<0.0001$	0.80
Waist circumference, cm	80.75	10.41	90.22	8.39	78.41	9.49	24.09	$P<0.0001$	1.41
Hip circumference, cm	94.32	6.61	97.88	7.02	93.99	6.48	6.84	$P<0.0001$	0.55
Body fat, %	27.78	7.46	31.05	7.62	27.48	7.38	5.48	$P<0.0001$	0.47
Haemoglobin, pg	14.06	1.60	14.33	1.63	14.02	1.59	3.75	$P=0.0002$	0.19
Haematocrit, %	42.54	4.09	43.06	4.20	42.47	4.07	2.75	$P=0.0061$	0.14
Mean corpuscular volume, fl	89.63	7.50	89.35	7.16	89.67	7.55	–0.80	NS	–0.04
Red blood cells,10^6/mm^3	4.77	0.54	4.84	0.54	4.76	0.54	2.78	$P=0.0054$	0.15
White blood cells,10^6/mm^3	5.84	1.60	6.36	1.66	5.77	1.57	7.04	$P<0.0001$	0.36
Mean corpuscular haemoglobin, pg	29.62	2.97	29.74	2.86	29.60	2.99	0.90	NS	0.05
Mean corpuscular-haemoglobin concentration, %	32.99	1.14	33.24	1.17	32.96	1.13	4.69	$P<0.0001$	0.24
Platelets, *1000/µl	248.52	59.81	246.50	63.20	248.80	59.33	–0.74	NS	–0.04

(continued)

Table 2. Continued.

	Total sample $n = 3368$		Metabolic syndrome						
			Yes $n = 409$		No $n = 2959$				
Biomarkers	Mean	SD	Mean	SD	Mean	SD	*t*	Statistical significance	ES (d)
Blood urea nitrogen, mg/dl	14.92	4.82	16.30	6.53	14.73	4.50	4.70	$P < 0.0001$	0.24
Uric acid, mg/dl	5.68	1.51	6.45	1.55	5.57	1.48	11.16	$P < 0.0001$	0.57
Total protein, g/dl	7.54	0.41	7.62	0.41	7.53	0.41	3.88	$P = 0.0001$	0.22
Albumin, g/dl	4.49	0.26	4.52	0.25	4.48	0.26	2.37	$P = 0.0176$	0.16
Globulin, g/dl	3.06	0.36	3.10	0.38	3.05	0.36	2.74	$P = 0.0062$	0.13
Glutamic-oxaloacetic transaminase, IU/l	24.19	12.38	27.70	17.36	23.71	11.44	4.51	$P < 0.0001$	0.23
Glutamic-pyruvic transaminase, IU/l	25.56	19.79	33.22	23.30	24.50	19.01	7.24	$P < 0.0001$	0.37
pH value	6.00	0.82	5.84	0.73	6.02	0.83	–4.72	$P < 0.0001$	–0.25
Bone mineral density	–0.76	1.03	–0.84	1.16	–0.75	1.02	–0.93	NS	–0.08

Student's *t*-test was applied to compare the differences in markers between subject groups with and without MetS; NS, no significant between-group difference ($P \geq 0.05$). ES, effect size: d = 0.2 refers to a small effect size; d = 0.5 refers to a medium effect size; and d = 0.8 refers to a large effect size.

Table 3. Adjusted relative risk (ARR) and risk score (RS) of selected metabolic components for metabolic syndrome according to the multiple Poisson regression model.

	Total sample $n=3368$		Metabolic syndrome: Yes $n=409$		Metabolic syndrome: No $n=2959$					
Selected metabolic components	*n*	%	*n*	%	*n*	%	ARR	95% confidence interval		RS
Waist circumference, cm										
Abnormal (male ≥90; female ≥80)	450	13.36	344	84.11	106	3.58	19.60	15.24	25.22	5
Normal (male <90; female <80)	2918	86.64	65	15.89	2853	96.42	1.00			1
Body mass index, kg/m^2										
Abnormal (≥24)	773	22.95	334	81.66	439	14.84	10.58	8.33	13.43	4
Normal (<24)	2595	77.05	75	18.34	2520	85.16	1.00			1
Triglyceride, mg/dl										
Abnormal (≥150)	723	21.47	317	77.51	406	13.72	10.22	8.22	12.72	4
Normal (<150)	2645	78.53	92	22.49	2553	86.28	1.00			1
Blood pressure, mmHg										
Abnormal (SBP ≥130; DBP ≥85)	193	5.73	190	46.45	3	0.10	7.46	6.36	8.75	4
Normal (SBP <130; DBP <85)	3175	94.27	219	53.55	2956	99.90	1.00			1
High-density lipoprotein cholesterol, mg/dl										
Abnormal (male <40; female <50)	323	9.59	122	29.83	201	6.79	3.74	3.12	4.47	3
Normal (male ≥40; female ≥50)	3045	90.41	287	70.17	2758	93.21	1.00			1
Fasting glucose, mg/dl										
Abnormal (≥100)	506	15.02	117	28.61	389	13.15	2.46	2.04	2.98	3
Normal (<100)	2862	84.98	292	71.39	2570	86.85	1.00			1

(continued)

Table 3. Continued.

	Total sample $n = 3368$		Metabolic syndrome							
			Yes $n = 409$		No $n = 2959$					
Selected metabolic components	*n*	%	*n*	%	*n*	%	ARR	95% confidence interval		RS
Uric acid, mg/dl										
Abnormal (male ≥7; female ≥6)	863	25.62	188	45.97	675	22.81	2.42	2.02	2.89	3
Normal (male <7; female <6)	2505	74.38	221	54.03	2284	77.19	1.00			1
Glutamic-pyruvic transaminase, IU/l										
Abnormal (>40)	366	10.87	94	22.98	272	9.19	2.35	1.91	2.88	3
Normal (≤40)	3002	89.13	315	77.02	2687	90.81	1.00			1
Glutamic-oxaloacetic transaminase, IU/l										
Abnormal (>40)	168	4.99	46	11.25	122	4.12	2.18	1.67	2.86	3
Normal (≤40)	3200	95.01	363	88.75	2837	95.88	1.00			1
Low-density lipoprotein cholesterol, mg/dl										
Abnormal (>130)	1363	40.47	197	48.17	1166	39.41	1.37	1.14	1.64	2
Normal (≤130)	2005	59.53	212	51.83	1793	60.59	1.00			1
Cholesterol, mg/dl										
Abnormal (>200)	1579	46.88	223	54.52	1356	45.83	1.35	1.13	1.62	2
Normal (≤200)	1789	53.12	186	45.48	1603	54.17	1.00			1

Table 4. Receiver operating characteristic curve analysis of selected metabolic components for metabolic syndrome.

Selected metabolic components		Area under the curve	Optimal cut-off point
Waist circumference, cm[a]	Female	0.87	79.49
	Male	0.84	89.48
Triglyceride, mg/dl[a]		0.85	150.35
High-density lipoprotein cholesterol, mg/dl[a]	Female	0.85	29.05
	Male	0.80	23.63
Body mass index, kg/m^2		0.80	25.07
Fasting glucose, mg/dl[a]		0.76	100.10
Blood pressure, mmHg[a]	Systolic	0.75	127.97
	Diastolic	0.74	85.02
Uric acid, mg/dl	Female	0.71	5.30
	Male	0.63	6.90
Glutamic-pyruvic transaminase, IU/l		0.66	26.00
Glutamic-oxaloacetic transaminase, IU/l		0.59	27.04
Cholesterol, mg/dl		0.55	225.96
Low-density lipoprotein cholesterol, mg/dl		0.54	133.95

[a]Current metabolic component used for diagnosing metabolic syndrome.

the RSs were calculated based on the ARR values and recorded as 2, 3, 4 or 5 when the ARR fell between 1 and 2, 2 and 4, 4 and 15, or was >15, respectively. Based on this rule, subjects with higher waist circumference values had their RS recorded as 5; those with higher BMI, TG and BP scored 4; those with abnormal HDL-C, FG, UA, GPT and GOT values had their RS recorded as 3; those with abnormal LDL-C and cholesterol scored 2; and those with normal values had their RS recorded as 1.

The ROC analysis using the selected 11 metabolic components to discriminate MetS showed that the discriminative validity of waist circumference was the highest, especially among women (AUC = 0.87; Table 4). TG, HDL-C, BMI, FG and BP also had good discriminative validity (AUC range, 0.74–0.85), whereas UA, GPT, GOT, cholesterol and LDL-C did not have good discriminative ability for MetS (AUC $\leq$ 0.71). This suggests that the five markers used as the current diagnostic criteria for MetS have the best discriminative ability of all metabolic components. BMI was not a match for waist circumference even though it showed good discriminative validity. In addition, according to the ROC analysis results in this current study, the optimal cut-off values of the current five markers were very close to the recommended values, and only the optimal cut-off value of HDL-C was lower than recommended.

To identify the best metabolic component combinations, this study used the current five-marker system as the basis and added one metabolic component at a time to form six combinations of six metabolic components each. After summing the RS of each metabolic component, a ROC analysis for MetS was performed and the results were compared with the current five-marker system. These current results showed that although the six combinations of six components all had good discriminative validity (AUC range, 0.967–0.976), they were still not as effective as the current five-marker system (AUC = 0.977; Table 5).

Table 5. Receiver operating characteristic curve analysis of metabolic syndrome by using the sum of risk scores of combinations of selected metabolic components.

Combinations of selected metabolic components	Area under the curve	Optimal cut-off point	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Current five items[a]	0.977	11.000	0.917	0.931	0.68	0.99
Current five items with waist circumference replaced by BMI	0.950	10.000	0.927	0.846	0.49	0.99
Current five items plus GOT	0.976	12.000	0.926	0.925	0.66	0.99
Current five items plus GPT	0.975	12.000	0.936	0.918	0.65	0.99
Current five items plus cholesterol	0.975	12.000	0.941	0.901	0.60	0.99
Current five items plus LDL-C	0.974	12.000	0.932	0.905	0.61	0.99
Current five items plus UA	0.969	12.000	0.936	0.889	0.57	0.99
Current five items plus BMI	0.967	12.001	0.946	0.843	0.49	0.99
All 11 items	0.954	19.999	0.903	0.861	0.51	0.98

[a]Including waist circumference, triglyceride, high-density lipoprotein cholesterol, fasting glucose and blood pressure.
BMI, body mass index; GOT, glutamic-oxaloacetic transaminase; GPT, glutamic-pyruvic transaminase; LDL-C, low-density lipoprotein cholesterol; UA, uric acid.

Even by including all 11 metabolic components into the analysis (AUC = 0.954), the results were not as effective as the current five-marker system or the six-marker combinations. Replacing waist circumference with BMI resulted in a drop in discriminative validity compared with the existing five-marker system (AUC = 0.950).

Discussion

Unlike some cross-sectional studies based on undiagnosed MetS data that could only provide temporal relationships,[28,29] this current study adopted a longitudinal approach to examine the discriminative ability of 11 physical and biochemical metabolic markers selected from a variety of potential components for the development of MetS, based on their associated RSs using a ROC curve analysis in a 5-year follow-up community cohort study. Although several studies in the Han Chinese population have used a similar design as the present study,[25,26,30] they mainly focused on middle-to-upper class people living in urban areas whose findings may not be representative of the general population. These previous studies also examined the relationship between MetS and single or few biomarkers, without taking current diagnostic components into account.[25,26,30] Not adjusting for the five diagnostic components results in a failure to further understand the contribution of individual markers in discriminating MetS in addition to the diagnostic criteria. Moreover, the relationships between study markers and MetS were more likely to be confounded by the diagnostic components.

Using the five markers used for current MetS diagnosis as the basis, the present study added one of six other metabolic markers (BMI, UA, GPT, GOT, cholesterol and LDL-C) to the diagnosis and found no increase in discriminative ability compared with the original five-marker system. Moreover, by replacing waist circumference with BMI, the current results showed that the predictability of waist circumference was greater. These current results suggest that despite the association between many physical and biochemical markers and MetS, the current five-marker diagnostic

system still represents the best combination for predicting the disease, and that adding other elements to the current diagnosis was unnecessary. This was particularly true for markers like UA, liver function markers (GPT and GOT) and other blood lipid markers (cholesterol and LDL-C).

It is worth noting that the optimal cut-off values obtained in this current study via the ROC curve analysis of the five markers used for current MetS diagnosis were consistent with the ATP III or IDF criteria.[1,23] The consistent optimal cut-off values and high AUC demonstrated the suitability and good discriminative ability of waist circumference, TG, BP, HDL-C and FG for MetS diagnosis. Only the optimal cut-off value of HDL-C (female $\geq$29 mg/dl; male $\geq$24 mg/dl) was lower than the current clinical standard (female $\geq$50 mg/dl; male $\geq$40 mg/dl). What accounts for the lower optimal cut-off value for HDL-C in this current study compared with the current clinical standard might be the older age of the Landseed Cohort (mean of 63.03 years for males; mean of 59.21 years for females). Mean HDL-C levels decrease with increasing age[31,32] and the role played by HDL-C in cardiovascular protection is, to a great extent, regulated by TG and LDL-C.[32–35] As a result, in this current study, HDL-C levels needed to reduce to a relatively low level to show a negative effect on MetS in this older aged sample. However, this hypothesis requires further validation through future studies as no similar finding has been reported in previously published research.

In addition, the present study replaced waist circumference with BMI as the MetS diagnostic criteria and found that whether compared against each other or evaluated by combining the other four markers, the ROC curve analysis results all showed that waist circumference had a higher discriminative ability for MetS than BMI. This result was consistent with some of the previous studies conducted using ROC curve analysis, which have demonstrated that the predictability of waist circumference is superior to BMI concerning CVD-related outcomes. For example, the Third National Health and Nutrition Examination Survey in the United States indicated that waist circumference surpassed BMI in predicting risk aspects of CVDs.[36,37] A previous study demonstrated that compared with BMI, central obesity (waist circumference) was a better discriminative marker for predicting hypertension, type 2 diabetes, and dyslipidaemia.[38]

A limitation of this study was the relatively old age of the sample, thus the study cohort differed from the demographic structure of the general population. As a result, the effects of different markers on MetS might be impacted. As this study used follow-up survey data from a single community, the generalizability of its results would require further validation by future studies.

In conclusion, considering the above limitation, this study confirmed that the current five-marker system has the best discriminative validity for MetS diagnosis, and although other physical and biochemical markers were likely capable of predicting MetS, their discriminative ability as diagnostic criteria is limited.

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Declaration of conflicting interest

The authors declare that there are no conflicts of interest.

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