

Population-based metabolic syndrome risk score and its determinants: The Isfahan Healthy Heart Program

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Background: Metabolic syndrome (MetSy), an important predisposing factor for the most of noncommunicable diseases, has become a global pandemic. Given different definitions used for the MetSy, recently using a score termed “continuous MetSy risk score (CMetSyS)” is recommended. The aim of this study was to provide a CMetSyS in a population-based sample of Iranian adults and to assess its determinants. **Materials and Methods:** We used the data of the baseline survey of a community trial entitled “the Isfahan health heart program.” The MetSy was defined according to the Revised National Cholesterol Education Program Third Adult Treatment Panel. All probable predictive models and their predictive performance were provided using leave-one-out cross-validated logistic regression and the receiver operation characteristic curve methods. Multiple linear regression was performed to assess factors associated with the CMetSyS. **Results:** The study population consisted of 8313 persons (49.9% male, mean age 38.54 ± 15.86 years). The MetSy was documented in 1539 persons (21.86%). Triglycerides and waist circumference were the best predictive components, and fasting plasma glucose had the lowest area under curve (AUC). The AUC for our best model was 95.36 (94.83-95.83%). The best predictive cutoff for this risk score was -1.151 with 89% sensitivity and 87.93% specificity. **Conclusion:** We provided four population-based leave-one-out cross-validated risk score models, with moderate to perfect predictive performance to identify the MetSy in Iranian adults. The CMetSyS had significant associations with high sensitive C-reactive protein, body mass index, leisure time, and workplace physical activity as well as age and gender.

Key words: Iran, metabolic syndrome, receiver operating characteristic curve, risk score

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INTRODUCTION

Metabolic syndrome (MetSy) is defined as a combination of adverse cardiovascular disease (CVD) and metabolic risk factors including abdominal obesity, dyslipidemia, hyperglycemia, and hypertension.^[1,2] A growing body of evidence documented that the MetSy is a risk factor for atherosclerotic CVD and type 2 diabetes mellitus (T2DM) incidence^[3-7] and mortality.^[8] It is a global epidemic and an exacerbating public health challenge worldwide.^[9]

Unfortunately, there is no consensus on the MetSy definition. Three definitions have been suggested by various organizations.^[10-12] The Revised National Cholesterol Education Program Third Adult Treatment Panel (RNCEP:ATPIII) definition requires three or more of the following components:

1. Waist circumference ([WC] ≥ 102 cm for men and ≥ 88 cm for women);

2. Increased triglycerides ([TG] ≥ 150 mg/dl or being under treatment);
3. Low, high-density lipoprotein cholesterol (HDL-C < 40 mg/dl for men and < 50 mg/dl for women or being under treatment);
4. Elevated blood pressure systolic blood pressure ([SBP] ≥ 130 mmHg, or diastolic blood pressure [DBP] ≥ 85 mmHg or receiving anti-hypertensive medications);
5. Increased fasting plasma glucose ([FPG] ≥ 100 mg/dl or treatment for hyperglycemia).^[13,14]

In the international diabetes federation definition, central obesity is necessary as a prerequisite (WC ≥ 94 cm for men and ≥ 80 cm for women) and in addition at least two of the raised TG, low HDL-C, elevated blood pressure (BP) and FPG.^[11] The recent joint interim statement definition requires the presence of three out of the five above mentioned components, but with considering national or regional-specific adoption for measure of the central obesity mainly WC.^[15]

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The prevalence and clinical usefulness of the MetSy are age, gender, and culture-dependent, augmenting with increasing age and more useful in males.^[16,17] In the middle east, the prevalence of the MetSy is more than western countries, with higher frequency in females than males.^[16,18] Studies showed about 21-45% of Iranian adult population suffer from MetSy.^[19,20]

Due to the high burden of the CVDs and T2DM, identifying individuals who are at higher risk for these disorders would be useful. As mentioned above, the MetSy is a risk factor for CVD and T2DM but during recent years using a continuous MetSy risk score (CMetSyS) is recommended instead of a yes/no definition.^[21-23]

Recently, Hsiao *et al.*, using data from a middle-aged cohort, published “the Chinese MetSy risk score.” They have used binary logistic regression and receiver operation characteristic (ROC) curve to construct their CMetSyS. During their study follow-up 30 of the 352 participants developed MetSy. They indicated TG and DBP have highest and lowest area under curve (AUC). They concluded that TG and WC are the most important variables, and their model could be useful for clinical screening for the MetSy.^[24]

The aim of this study was to construct a CMetSyS in an Iranian adult population and to provide an evaluation of the predictive performance of the CMetSyS to identify individuals with MetSy. Our second objective was to determine factors associated with CMetSyS.

MATERIALS AND METHODS

The Isfahan Healthy Heart Program (IHHP) data were used in this cross-sectional analysis. IHHP is a comprehensive, community-based healthy lifestyle program with a reference area; the details are published elsewhere.^[19,25] Briefly, data were collected from three communities located in the central area of Iran including: Isfahan, Najaf-Abad, and Arak.

Ethics committees and other relevant national regulatory organizations approved the study. Written informed consent was obtained from participants after full explanation of the study protocol.

Five to 10% of households were selected using a random two-stage clustered sampling method. During survey, data from 8313 individuals aged ≥ 19 years (one random selected adult within each household) was collected in Isfahan, Najafabad, and Arak. The participants were interviewed to complete validated questionnaires containing questions on demography, socioeconomic status, smoking behavior, physical activity, nutritional habits, and other behavior regarding CVD. In clinics, anthropometric measurements

were conducted by calibrated instruments and under standard protocols.

Participants were asked to fast for 12 h prior to the examinations. High-sensitivity C-reactive protein (hs-CRP) for 7087 participants, FPG, total cholesterol (T-Chol), HDL-C, low-density lipoprotein cholesterol (LDL-C), and TG were assessed. Two hours postload plasma glucose (2 hPG) was examined, as well. All blood samples were examined in the central laboratory of the Isfahan cardiovascular research center (a collaborating center of the World Health Organization), with adherence to external national and international quality control.

In this study, although binary MetSy was defined according to the RNCEP: ATPIII and its criteria for the components of the MetSy, but after comparing the AUC from models including each components as a categorical or continuous independent variable, we decided to use continuous values of the components of the MetSy during model building.

For approaching elevated BP and for reducing the number of model parameters, mean arterial pressure (MAP) was used. It was calculated using the following equation:

$$\text{MAP} = ([\text{SBP} - \text{DBP}] / 3) + \text{DBP}^{[24]}$$

Then, we compared model including only MAP with which one consists of MAP and SBP using likelihood ratio test (LRT) ($P = 0.041$) and also AUC using DeLong method ($P = 0.05$). This comparison shows no statistical significance at 0.01. Therefore, we used MAP to consider BP during modeling.

Using logistic regression with a binary outcome, based on modified National Cholesterol Education Program (NCEP): ATPIII MetSy definition for Asian populations, including gender and age and also one of the MAP, WC, T-Chol, HDL-C, TG, hip circumference (HC), WC to HC ratio (waist to hip circumferences), body mass index (BMI), FPG, and 2 hPG as independent variables, we predicted the probability of presence of the MetSy. Then AUC and its binomial 95% confidence interval (CI) were calculated for each model.

Considering the value of AUC and clinical practicability, more useful predictors were selected and modeled in different approaches.

Finally, we construct four different models as following list:

- Model 1: Including informative blood glucose measurement (FBS).
- Model 2: Including powerful nonlaboratory measurements (WC, BMI, and MAP).

- Model 3: Including main serum lipids measurements (TG, HDL-C, and LDL-C).
- Model 4 (full model): Including all components of MetSy (FPG, HDL-C, WC, MAP, and TG).

To model building and validation, we conducted user stepwise selection (using LRT) and leave-one-out cross-validation methods (using Crossval macro^[26] for STATA statistical software) (release: 11.2; StataCorp, TX, USA). For each model, the AUC and its 95% CI was calculated and compared (DeLong method) with its sub-models which were included less independent variables and also a full model.

We calculated the probability of the MetSy for each person using following formula only for Model 4:

$$Pr = 1/(1 + e^{-x})$$

where x represent the suggested CMetSyS.

After constructing the CMetSyS, by using Multiple linear regression, we assessed linear relationship of the CMetSyS with smoking status, percentiles of the CRP value (hs-CRP), global dietary index, total, leisure time, homework, and workplace physical activity scores, and BMI. We compared determinants of the MetSy as a binary outcome with its determinants when it was defined as a continuous risk score. To do this, we fitted a logistic regression with statistically significant determinants of the CMetSyS as its independent variables. Then statistical significance was used to compare those determinants.

All statistical analyses were conducted using STATA statistical software (release: 11.2; StataCorp, TX, USA).

RESULTS

Mean and standard deviation of age for men were 38.5 (15.9) and for women were 39.3 (15.3). Total prevalence of the MetSy was 21.9%, 29.0% and 14.7% in females and males, respectively. More descriptive data are shown in Table 1. Percentages of abnormality of each component of the MetSy were estimated based on NCEP: ATP III criteria. These estimations are displayed in Table 2 divided for gender.

Percentages of subjects with 0, 1, 2, 3, 4 or 5 abnormal component were calculated by gender. These percentages were 14.7, 29.3, 27.0, 19.7, 7.7, and 1.5 for females and 28.8, 30.9, 25.7, 10.6, 3.7, and 0.5 for males, respectively.

The AUC of the models including both gender and age and one or more independent variables and its binomial 95% CI are presented in Table 3. It also illustrates the results of the comparison of each AUC with the next one based on DeLong method. The statistical significance level of LR test

Table 1: The metabolic description of study participants

Variables	Mean ± SD		P	Total Mean ± SE
	Females	Males		
Age (year)	39.6±15.3	38.6±15.9	0.01	38.6±15.6
TG (mg/dL)	141.2±94.5	158.1±103.3	<0.01	145.8±99.3
HDL-C (mg/dL)	46.9±10.7	41.5±9.6	<0.01	44.3±10.5
LDL-C (mg/dL)	112.6±29.8	107.8±27.6	<0.01	109.7±28.8
T-Chol (mg/dL)	197.3±42.5	187.8±39.9	<0.01	191.5±41.4
WC (cm)	91.0±13.2	89.2±11.5	<0.01	89.8±12.4
BMI (kg/m ²)	26.7±4.9	24.9±4.1	<0.01	25.7±4.6
SBP (mm Hg)	112.0±19.6	116.0±17.5	<0.01	113.6±18.7
DBP (mm Hg)	73.2±11.3	75.9±9.8	<0.01	74.1±10.6
Total physical activity (MET-h/week)	613.8±294.3	731.0±453.7	<0.01	675.4±384.6
hs-CRP (mg/L)	3.3±2.9	3.3±3.0	0.33	3.3±3.0
GDI	0.76±0.3	0.82±0.3	<0.01	0.8±0.3
FPG (mg/dL)	89.5±24.9	89.9±25.0	0.52	86.8±24.9
2 hPG (mg/dL)	107.6±35.7	104.4±37.4	<0.01	106.5±36.6

TG = Triglycerides; HDL-C = High-density lipoprotein cholesterol; LDL-C = Low Density lipoprotein cholesterol; T-Chol = Total cholesterol; WC = waist circumference; BMI = Body mass index; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; hs-CRP = High-sensitivity C-reactive protein; GDI = Global dietary index; FPG = fasting plasma glucose; 2 hPG = Two hours postload plasma glucose; MET = Metabolic equivalent task; SD = Standard deviation; SE = Standard error

Table 2: Gender-divided percentages of abnormality of the components of the MetSy (according to NCEP: ATP III) among study participants

Component	Percentage		P	Total
	Females	Males		
TG (mg/dL)	31.6	40.0	<0.01	35.8
HDL-C (mg/dL)	63.0	46.2	<0.01	54.6
WC (cm)	56.8	12.6	<0.01	34.7
SBP (mm Hg)	21.7	25.2	<0.01	23.4
FPS (mg/dL)	7.3	6.6	0.18	7.0

TG = Triglycerides; HDL-C = High-density lipoprotein cholesterol; WC = Waist circumference; SBP = Systolic blood pressure; FPG = Fasting plasma glucose; MetSy = Metabolic syndrome; NCEP: ATP III = National cholesterol education program third adult treatment panel

to assessing the goodness of fit of each model comparing with the same, but without underlined variable in the first column presented in the last column in this table.

Table 4 shows coefficient, odds ratio, and statistical significance level of each variable in the best-fitted logistic models [which been bold in Table 3] to predict the probability of presence of the MetSy in Iranian adults. These models are presented in Table 4 with ascending ranks according to the AUC. The cross-validated (leave-one-out) estimates of AUC for Models 1 to 4 were 0.78, 0.88, 0.90, and 0.95, respectively.

Although four separate models were fitted, but as an example we calculated the X (where probability of presence of the MetSy is $Pr = 1/(1 + e^{-X})$.) using the best one (Model 4). For calculations, we used following equation where all except gender are continuous variables

Table 3: AUC and its 95% binomial CI for each model and statistical significance of their AUC and goodness of fit

Added variable	AUC (95% binomial CI)	P (DeLong)	P (LRT)
Gender (male [2]/female [1])	0.60 (0.59-0.62)	<0.01**	<0.01
Age	0.74 (0.73-0.75)	<0.01**	<0.01
Gender, age, 2 hPG	0.76 (0.75-0.77)	<0.01**	<0.01
Gender, age, LDL-C	0.76 (0.75-0.77)	<0.01**	<0.01
Gender, age, T-Chol	0.78 (0.77-0.79)	0.01**	<0.01
Gender, age, FPS	0.78 (0.77-0.79)	<0.01**	<0.01
Gender, age, SBP	0.81 (0.80-0.82)	0.05**	<0.01
Gender, age, MAP	0.81 (0.8-0.82)	0.92**	<0.01
Gender, age, WHR	0.81 (0.80-0.82)	0.17**	<0.01
Gender, age, HC	0.82 (0.81-0.83)	<0.01**	<0.01
Gender, age, BMI	0.84 (0.83-0.84)	0.08**	<0.01
Gender, age, HDL-C	0.85 (0.84-0.86)	0.06**	<0.01
Gender, age, WC	0.86 (0.85-0.87)	0.01**	<0.01
Gender, age, TG	0.88 (0.87-0.89)	-	<0.01
Gender, age, HDL-C, LDL-C	0.86 (0.85-0.87)	<0.01*	<0.01
Gender, age, HDL-C, LDL-C, T-Chol	0.88 (0.87-0.89)	<0.01*	<0.01
Gender, age, HDL-C, LDL-C, TG	0.90 (0.89-0.91)	<0.01*	<0.01
Gender, age, WC, BMI	0.86 (0.85-0.87)	<0.01	<0.01
Gender, age, BMI, WC, HC	0.86 (0.85-0.87)	0.24*	0.02*
Gender, age, BMI, WC, WHR	0.86 (0.85-0.87)	0.43*	0.02*
Gender, age, FPS, 2 hPG	0.77 (0.76-0.78)	<0.01	<0.01
Gender, age, BMI, WC, MAP	0.88 (0.87-0.89)	<0.01	<0.01
Gender, age, TG, WC	0.915 (0.91-0.92)	<0.01	<0.01
Gender, age, TG, WC, HDL-C	0.93 (0.926-0.938)	<0.01	<0.01
Gender, age, TG, WC, HDL-C, MAP	0.948 (0.94-0.953)	<0.01	<0.01
Gender, age, WC, HDL-C, TG, MAP, FPG	0.954 (0.948-0.958)	<0.01 Compared to all above models	

AUC = Area under curve; CI = Confidence interval; LRT = Likelihood ratio test; TG = triglycerides; HDL-C = High-density lipoprotein cholesterol; LDL-C = Low density lipoprotein cholesterol; T-Chol = Total cholesterol; WC = Waist circumference; BMI = Body mass index; SBP = Systolic blood pressure; FPG = Fasting plasma glucose; 2 hPG = Two hours postload plasma glucose; MAP = Mean arterial pressure; WHR = Ratio of waist to hip circumferences; HC = Hip circumference; FPS = Fasting plasma sugar; **Compared with the next value in the lower row; *Compared with one which is different in the case of inclusion of underlined variable in the first column

with units mentioned in Table 1, gender is a binary variable with one and two codes representing female and male, respectively.

$$X = -14.43465 + (-0.13 \times \text{HDL-C}) + (0.01 \times \text{TG}) + (0.03 \times \text{FPS}) + (0.11 \times \text{WC}) + (0.09 \times \text{MAP}) + (0.02 \times \text{age}) + (-2.83 \times \text{gender}).$$

The minimum and maximum score of the X were -12.6 and 14.5, respectively. Best cut point of X for classification of the MetSy (yes/no) was -1.15 with 89% sensitivity and 87.9% specificity and 88.2% correct classification. The AUC and ROC curve for each of four models mentioned in Table 4 are illustrated in Figure 1.

We also assessed the probable determinants of the CMetSyS constructed by Model 4. Table 5 shows the determinants of the CMetSyS (X) determined by linear regression and their coefficient, and also P-values provided by logistic regression.

DISCUSSION

In this study, we constructed and validated four CMetSyS to identify the MetSy in Iranian adults. Then we determined

determinants of the CMetSyS. To the best of our knowledge, this is the first study of its kind in a Middle-Eastern adult population.

Considering some circumstances in which clinicians or epidemiologists do not have values on some components of MetSy, building some CMetSyS applicable for these conditions would be of use. First, when we have only age, gender and FPG, the model had lower discriminative power but still plausible AUC^[27] (78.1 [95% CI: 77.1-79.1]). Although 2 hPG added to this model, but it had no statistically significant added value on AUC or goodness of fit. The second ones provide CMetSyS for conditions in which we have nonlaboratory variables, e.g., BMI, WC, and MAP. The next model was provided for circumstances in which only serum lipid profile and TG were considered. If we have values of each five components of MetSy, the Model 4 will be the best one.

Our study shows that TG and WC are the number one and two contributors in presence of the MetSy. HDL-C and MAP are in third and fourth order, and the last one is FPG. Hsiao *et al.*, found TG and WC as more important components of MetSy.^[24] Based on our findings, HDL-C

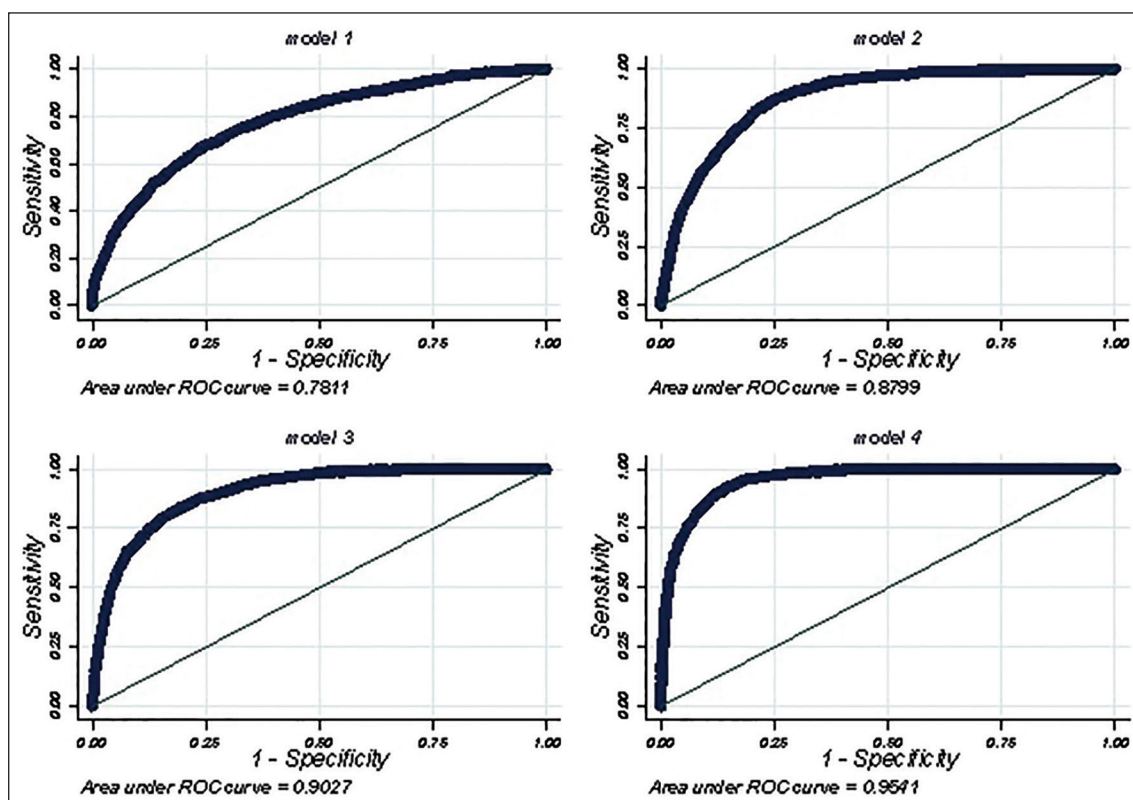


Figure 1: The receiver operation characteristic curve and area under curve for each of suggested models to construct continuous metabolic syndrome risk score for Iranian adults. Model 1: including informative blood glucose measurement (fasting blood sugar). Model 2: including powerful nonlaboratory measurements (waist circumference [WC], body mass index and mean arterial pressure [MAP]). Model 3: including main serum lipids measurements (triglycerides, high-density lipoprotein cholesterol [HDL-C] and low-density lipoprotein cholesterol). Model 4: including all components of the MetSy (fasting plasma glucose, HDL-C, WC, MAP, and TG)

has the same rank as in Hsiao *et al.* but FPG and BP do not have the same importance as in their study. In our study, the predictive performance of MAP had no statistically significant difference with SBP. However, one probable reason for this distinction may be because of considering the BP as MAP in our study and as SBP and DBP in the study of Hsiao *et al.* Despite ranks for importance of BP as well as other components, the AUC for BP in our study was 81.3 (80.4-0.82.2) and 59.5 (50.8-68.3) in their study. Considering the follow-up nature of data that used in Hsiao *et al.* (provide ability to predict MetSy for healthy people in the future) and cross-sectional nature of data which we used (provide ability to identifying peoples with MetSy at this time), this difference could provide probable evidence on more predictive performance of BP and other components for discriminate the present MetSy than for its future incidence.

Considering our full model, this study provides approval evidence on independent predictive performance of TG and WC to discriminate the MetSy. This finding confirms the Hsiao *et al.* results.^[24] All over again, our best model demonstrates independency of influence of other components of the MetSy to estimate the risk of presence of the MetSy. One possible reason for this discrepancy may be a large difference

between the sample size of two studies as well as the possible effects of regional and ethnical differences. In concordance with our findings, there are some evidences on the presence of gradient relationship between the CMetSyS and number of abnormal components of MetSy.^[21,27]

Although univariate study results showed statistically significant differences between those with MetSy and healthy participants in terms of all type of physical activity, the CMetSyS had significant relationships with leisure time and workplace physical activity, but the corresponding figure was not significant for homework physical activity and total physical activity score. Against univariate results, logistic regression showed no statistical association between the MetSy and all types of physical activities. These findings demonstrate two key points: First, the importance of leisure time and workplace physical activities and second, according to more analysis (not shown), probable confounding effect of gender on those effects when using yes/no definition for the MetSy. The significant association of the CMetSyS with leisure time physical (LTPHYA) was shown earlier in American children.^[28] Hence, we could conclude CMetSyS in adults or children has a probable relationship with LTPHYA activity.

Table 4: Best-fitted logistic models to predict presence of the MetSy in Iranian adults, sorted based on the AUC from lowest to highest

Model	Variables	Coefficient (95% CI)	OR (95% CI)	P
Model 1	Constant	-3.81 (-4.15 to -3.47)	-	<0.01
	Gender (male/female)	-1.01 (-1.14 to -0.88)	0.37 (0.32-0.42)	<0.01
	Age	0.042 (0.038 to 0.046)	1.04 (1.04-1.05)	<0.01
	FPG	0.024 (0.021 to 0.027)	1.02 (1.02-1.03)	<0.01
Model 2	Constant	-15.01 (-15.89 to -14.12)	-	<0.01
	Gender (male/female)	-1.08 (-1.23 to -0.93)	0.34 (0.29-0.39)	<0.01
	Age	0.02 (0.02 to 0.03)	1.02 (1.015-1.03)	<0.01
	BMI	0.032 (0.01 to 0.06)	1.03 (1.01-1.02)	0.01
	WC	0.09 (0.08 to 0.10)	1.09 (1.08-1.10)	<0.01
	MAP	0.06 (0.05 to 0.10)	1.06 (1.05 1.07)	<0.01
Model 3	Constant	0.49 (-0.05 to 1.04)	-	<0.01
	Gender (male/female)	-2.02 (-2.20 to -1.90)	0.13 (0.11-0.16)	<0.01
	Age	0.052 (0.0472 to 0.057)	1.054 (1.048-1.06)	0.01
	HDL-C	-0.104 (-0.114 to -0.094)	0.90 (0.89-0.91)	<0.01
	LDL-C	0.014 (0.011 to 0.017)	1.014 (1.011-1.02)	<0.01
	TG	0.010 (0.009 to 0.011)	1.010 (1.009-1.011)	<0.01
Model 4	Constant	-14.44 (-15.7 to -13.20)	-	<0.01
	Gender (male/female)	-2.83 (-3.06 to -2.6)	0.06 (.05-0.07)	<0.01
	Age	0.02 (0.01 to 0.03)	1.02 (1.01-1.03)	<0.01
	FPG	0.025 (0.021 to 0.029)	1.026 (1.021-1.030)	0.01
	MAP	0.09 (0.08 to 0.10)	1.09 (1.08-1.10)	<0.01
	TG	0.01 (0.009 to 0.011)	1.010 (1.009-1.011)	<0.01
	HDL-C	-0.13 (-0.14 to -0.12)	0.88 (0.87-0.89)	<0.01
	WC	0.11 (0.10 to 0.12)	1.11 (1.10-1.12)	<0.01

MetSy = Metabolic syndrome; AUC = Area under curve; CI = Confidence interval; OR = Odds ratio; BMI = Body mass index; MAP = Mean arterial pressure; TG = Triglycerides; HDL-C = High-density lipoprotein cholesterol; WC = Waist circumference; FPG = Fasting plasma glucose; LDL-C = Low density lipoprotein cholesterol

Table 5: Determinants of the CMetSyS for Iranian adults and their ORs from logistic regression

Determinant	Linear regression			Logistic regression	
	Coefficient	T-statistic	P	OR	P
Gender	-0.93	-12.03	<0.01	0.55	<0.01
Age	0.07	36.89	<0.01	1.05	<0.01
WPPHYA	-0.005	-4.10	<0.01	0.99	0.240
LTPHYA	-0.003	-3.02	<0.01	1.00	0.450
BMI	0.06	57.35	<0.01	1.04	<0.01
hs-CRP	0.003	2.75	<0.01	1.00	0.074
Intercept	-7.19	-49.96	<0.01	-	-

Estimated R² for linear regression model = 0.51. WPPHYA = Work place physical activity; LTPHYA = Leisure time physical activity; BMI = Body mass index; hs-CRP = High-sensitivity C-reactive protein; CMetSyS = Continuous MetSy risk score; OR = Odds ratio

Linear regression also showed a significant association between the CMetSyS and BMI or hs-CRP percentiles. This finding is in concordance with some other studies.^[28,29] Although we do not have any confirmation on the association of MetSy with hs-CRP if accept present evidence from other studies, comparing results of logistic regression and linear regression could provide some evidence on using the CMetSyS instead of yes/no definition. Alexander *et al.*^[29] showed there is also a relationship between obesity and hs-CRP level and other authors revealed the relationship of hs-CRP and the

MetSy.^[30,31] These findings are in agreement with studies on risk factors of CVDs.^[32]

In this study, our limitation was cross-sectional context of the study although most risk score studies are cross-sectional, but the goal of risk score studies is prediction of future disorder and this need cohort designs. However, considering the concordance of our findings with which in other studies with cohort designs, it can be suggested that this limitation had no or a very weak effect on our study conclusion.

CONCLUSION

Four generalizable continuous risk score models with plausible predictive performance to identify the MetSy in Iranian adults were generated. The best CMetSyS provided in this study had a significant relation with hs-CRP, BMI, leisure time, and workplace physical activity as well as age and gender. Although we provided a practicable CMetSyS to predict the MetSy in Iranian adults but for better predictions follow-up studies are needed.

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AUTHOR'S CONTRIBUTIONS

SMH contributed in the design of the study, revising the draft and approval of the final version of the manuscript, and agreed for all aspects of the work. RK contributed in the design of the study, revising the draft and approval of the final version of the manuscript, and agreed for all aspects of the work. HMV contributed in the design of the study, data analysis, writhing and revising the draft and approval of the final version of the manuscript, and agreed for all aspects of the work. MM contributed in the data analysis, revising the draft and approval of the final version of the manuscript, and agreed for all aspects of the work. NS contributed in the design of the main study, revising the draft and approval of the final version of the manuscript, and agreed for all aspects of the work. SA contributed in the design of the main study, revising the draft and approval of the final version of the manuscript, and agreed for all aspects of the work.

REFERENCES

1. Reaven GM. The metabolic syndrome: Time to get off the merry-go-round? *J Intern Med* 2011;269:127-36.
2. Parikh RM, Mohan V. Changing definitions of metabolic syndrome. *Indian J Endocrinol Metab* 2012;16:7-12.
3. Ford ES. Risks for all-cause mortality, cardiovascular disease, and diabetes associated with the metabolic syndrome: A summary of the evidence. *Diabetes Care* 2005;28:1769-78.
4. Hanson RL, Imperatore G, Bennett PH, Knowler WC. Components of the "metabolic syndrome" and incidence of type 2 diabetes. *Diabetes* 2002;51:3120-7.
5. Gupta R. Metabolic syndrome as a marker of risk in type 2 diabetes. *Indian J Med Res* 2009;129:481-4.
6. Kalantzi K, Korantzopoulos P, Tzimas P, Katsouras CS, Goudevenos JA, Milionis HJ. The relative value of metabolic syndrome and cardiovascular risk score estimates in premature acute coronary syndromes. *Am Heart J* 2008;155:534-40.
7. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, *et al.* The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. *JAMA* 2002;288:2709-16.
8. Hildrum B, Mykletun A, Dahl AA, Midthjell K. Metabolic syndrome and risk of mortality in middle-aged versus elderly individuals: The Nord-Trøndelag Health Study (HUNT). *Diabetologia* 2009;52:583-90.
9. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. *Lancet* 2005;365:1415-28.
10. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. 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.
11. Alberti KG, Zimmet P, Shaw J, IDF Epidemiology Task Force Consensus Group. The metabolic syndrome: A new worldwide definition. *Lancet* 2005;366:1059-62.
12. Balkau B, Charles MA, Drivsholm T, Borch-Johnsen K, Wareham N, Yudkin JS, *et al.* Frequency of the WHO metabolic syndrome in European cohorts, and an alternative definition of an insulin resistance syndrome. *Diabetes Metab* 2002;28:364-76.
13. Alkerwi A, Donneau AF, Sauvageot N, Lair ML, Scheen A, Albert A, *et al.* Prevalence of the metabolic syndrome in Luxembourg according to the Joint Interim Statement definition estimated from the ORISCAV-LUX study. *BMC Public Health* 2011;11:4.
14. Lin JW, Chang YC, Li HY, Chien YF, Wu MY, Tsai RY, *et al.* Cross-sectional validation of diabetes risk scores for predicting diabetes, metabolic syndrome, and chronic kidney disease in Taiwanese. *Diabetes Care* 2009;32:2294-6.
15. Alberti KG, Eckel RH, Grundy SM, Zimmet PZ, Cleeman JJ, Donato KA, *et al.* Harmonizing the metabolic syndrome: A joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* 2009;120:1640-5.
16. Hollman G, Kristenson M. The prevalence of the metabolic syndrome and its risk factors in a middle-aged Swedish population – Mainly a function of overweight? *Eur J Cardiovasc Nurs* 2008;7:21-6.
17. DECODE Study Group. Does diagnosis of the metabolic syndrome detect further men at high risk of cardiovascular death beyond those identified by a conventional cardiovascular risk score? The DECODE Study. *Eur J Cardiovasc Prev Rehabil* 2007;14:192-9.
18. Delavari A, Forouzanfar MH, Alikhani S, Sharifian A, Kelishadi R. First nationwide study of the prevalence of the metabolic syndrome and optimal cutoff points of waist circumference in the Middle East: The national survey of risk factors for noncommunicable diseases of Iran. *Diabetes Care* 2009;32:1092-7.
19. Sarrafzadegan N, Kelishadi R, Baghaei A, Hussein Sadri G, Malekafzali H, Mohammadifard N, *et al.* Metabolic syndrome: An emerging public health problem in Iranian women: Isfahan Healthy Heart Program. *Int J Cardiol* 2008;131:90-6.
20. Borzouei S, Hosseinpanah F, Azizi F. Agreement level of definitions of the metabolic syndrome by modified ATP III and IDF with insulin resistance in the lipid and glucose study (TLGS). *Iran J Endocrinol Metab* 2009;10:435-43.
21. Wijndaele K, Beunen G, Duvigneaud N, Matton L, Duquet W, Thomis M, *et al.* A continuous metabolic syndrome risk score: Utility for epidemiological analyses. *Diabetes Care* 2006;29:2329.
22. Kahn R, Buse J, Ferrannini E, Stern M, American Diabetes Association, European Association for the Study of Diabetes. 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.
23. Eisenmann JC. On the use of a continuous metabolic syndrome score in pediatric research. *Cardiovasc Diabetol* 2008;7:17.
24. Hsiao FC, Wu CZ, Hsieh CH, He CT, Hung YJ, Pei D. Chinese metabolic syndrome risk score. *South Med J* 2009;102:159-64.
25. Sarraf-Zadegan N, Sadri G, Malek Afzali H, Baghaei M, Mohammadi Fard N, Shahrokhi S, *et al.* Isfahan Healthy Heart Programme: A comprehensive integrated community-based programme for cardiovascular disease prevention and control. Design, methods and initial experience. *Acta Cardiol* 2003;58:309-20.
26. Thomsson RC. *Crossval.ado: A Macro for Stata* (updated February 12, 2000, by James Tonascia). College Station, TX: StataCorp, 2000. Available from: <http://www.biostat.jhsph.edu/~ejohnson/regression/crossval.ado>. [Last cited on 2012 May 21].
27. Eisenmann JC, Laurson KR, DuBose KD, Smith BK, Donnelly JE. Construct validity of a continuous metabolic syndrome score in children. *Diabetol Metab Syndr* 2010;2:8.
28. Okosun IS, Boltri JM, Lyn R, Davis-Smith M. Continuous metabolic syndrome risk score, body mass index percentile, and leisure

- time physical activity in American children. *J Clin Hypertens (Greenwich)* 2010;12:636-44.
29. Alexander CM, Landsman PB, Grundy SM. The influence of age and body mass index on the metabolic syndrome and its components. *Diabetes Obes Metab* 2008;10:246-50.
30. Oliveira AC, Oliveira AM, Adan LF, Oliveira NF, Silva AM, Ladeia AM. C-reactive protein and metabolic syndrome in youth: A strong relationship? *Obesity (Silver Spring)* 2008;16:1094-8.
31. Yang T, Chu CH, Hsieh PC, Hsu CH, Chou YC, Yang SH, *et al.* C-reactive protein concentration as a significant correlate for metabolic syndrome: A Chinese population-based study. *Endocrine* 2013;43:351-9.
32. Lin G, Li Y, Jaiteh L, Han C. C-reactive protein, metabolic syndrome and cardiovascular disease. *J Metab Syndr* 2012;1:e106.

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