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ORIGINAL ARTICLE

Clustering of leptin and physical activity with components of metabolic syndrome in Iranian population: an exploratory factor analysis

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Abstract Metabolic syndrome (MetS), manifested by insulin resistance, dyslipidemia, central obesity, and hypertension, is conceived to be associated with hyperleptinemia and physical activity. The aim of this study was to elucidate the factors underlying components of MetS and also to test the suitability of leptin and physical activity as additional components of this syndrome. Data of the individuals without history of diabetes mellitus, aged 25–64 years, from third national surveillance of risk factors of non-communicable diseases (SuRFNCD-2007), were analyzed. Performing factor analysis on waist circumference, homeostasis model assessment of insulin resistance, systolic blood pressure, triglycerides (TG) and high-density lipoprotein cholesterol (HDL-C) led to extraction of two factors which explained around 59.0% of the total variance in both genders. When TG and HDL-C were replaced by TG to HDL-C ratio, a single factor was obtained. In contrast to physical activity, addition of leptin was consistent with one-factor structure of MetS and improved the ability of suggested models to identify obesity (BMI $\geq$ 30 kg/m^2, $P < 0.01$), using receiver-operator characteristics curve analysis. In general, physical activity loaded on the first identified factor. Our study shows that one underlying factor structure of MetS is also plausible and the inclusion of leptin does not interfere with this structure. Further, this study suggests that physical activity influences MetS components via modulation of the main underlying pathophysiologic pathway of this syndrome.

Keywords Metabolic syndrome · Factor analysis · Leptin and physical activity

Abbreviations

BMI	Body mass index
CDC	Center for disease control
GPAQ	Global physical activity questionnaire
HDL-C	High-density lipoprotein cholesterol
HOMA-IR	Homeostasis model assessment of insulin resistance
LDL-C	Low-density lipoprotein cholesterol
MET	Metabolic equivalent
MetS	Metabolic syndrome
SuRFNCD-2007	Third national surveillance of risk factors of non-communicable diseases conducted in 2007
SBP	Systolic blood pressure

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TG	Triglycerides
TG/HDL-C	Triglycerides to high-density lipoprotein cholesterol
TPA	Total physical activity

Introduction

Metabolic syndrome (MetS) refers to the clustering of coronary heart disease and diabetes mellitus risk factors [1]. Several definitions of MetS have been proposed, but all include insulin resistance or glucose intolerance, dyslipidemia, central obesity, and elevated blood pressure. Hyperleptinemia, hyperuricemia, and elevated levels of inflammatory markers (e.g., C-reactive protein) have also been suggested as components of MetS [2–5]. There is also an inverse association between physical activity and MetS [6, 7]. Further knowledge regarding the clustering of MetS components can help clinicians to implement preventive and interventional efforts for individuals at risk for cardiovascular disease and type 2 diabetes mellitus.

Due to strong interrelationships between components of MetS, establishing independent associations using standard multivariate statistical models is difficult [8, 9]. Factor analysis is potentially a way of circumventing this problem by explaining the correlation between the components of the syndrome in terms of a small set of uncorrelated latent factors accounting for most of the variance. The intercorrelations between MetS components can be attributable to a single or multiple pathophysiologic mechanisms [9]. In factor analysis each extracted factor corresponds to a single underlying pathophysiologic pathway [8]; therefore, factor analysis is well suited for identifying the underlying structure of MetS components [8, 9]. Review of previous studies shows that from 1 to 7 factors have been extracted through factor analysis, revealing large discrepancies between outcomes of different studies [2–5, 10–13]. This phenomenon can be a result of the fact that number and nature of components in different studies has been chosen apparently arbitrarily. Since factor analysis extracts factors due to the interrelatedness of measured variables, using two or more measures for the same trait (e.g., systolic blood pressure [SBP] and diastolic blood pressure) leads to find more factors than expected [14].

Adipocytes produce a protein hormone, leptin, which reflects the body's fat content [15]. It has been demonstrated that MetS, obesity, and cardiovascular disease are all linked to leptin [16]. Further, insulin sensitivity is related to the interindividual variations in plasma leptin concentrations [17]. Review of previous studies that have performed factor analysis on the components of MetS together with leptin shows that leptin usually loads on the first extracted factor [2, 3, 5].

There is also interaction between physical activity and MetS. Previous cross-sectional and prospective studies suggest that physical activity protects against the development of diabetes [18], cardiovascular disease [19], and MetS [6, 7].

In this study for the first time we performed sex-specific factor analysis on the components of MetS in a large representative sample of Iranian adult population. Also we evaluated the implication of adding leptin and physical activity as additional components of MetS.

Results

Descriptive statistics

Sex-specific principal characteristics of the study population are presented in Table 1. The mean age ± SEM of men and women was 36.2 ± 0.3 and 38.0 ± 0.3 years, respectively ($P > 0.05$). Around one-fifth of men and one-fourth of women had elevated LDL-C levels ($P < 0.001$). Women were engaged more than men in the category of low physical activity (48.5 vs. 29.8, $P < 0.001$) and had higher prevalence of obesity (26.6 vs. 13.1, $P < 0.001$).

Univariate associations

The correlation matrix between the variables of interest is shown in Table 2. Total physical activity (TPA) was associated with HOMA-IR, leptin, and conventional variables of MetS in both genders. HDL-C was not associated

Table 1 Principal characteristics of the study population

	Men ($n = 1483$)	Women ($n = 1518$)
Age (years)	36.2 ± 0.3	38.0 ± 0.3
BMI (kg/m^2)	24.9 ± 0.1	26.8 ± 0.1
Waist circumference (cm)	87.3 ± 0.3	86.8 ± 0.3
HOMA-IR (unites)	2.19 ± 0.07	2.21 ± 0.04
TG (mg/dl)	156.1 ± 2.7	139.2 ± 2.0
HDL-C (mg/dl)	34.9 ± 0.3	39.3 ± 0.3
LDL-C (mg/dl)	209.4 ± 12.8	166.5 ± 7.9
SBP (mmHg)	125.0 ± 0.3	120.6 ± 0.4
Leptin (ng/ml)	4.0 ± 0.1	10.8 ± 0.2
TPA (MET-minutes/week)	6214.3 ± 167.9	2265.0 ± 72.7
LDL-C ≥ 160 mg/dl (%)	18.1	25.6
BMI ≥ 30 kg/m^2 (%)	13.1	26.6
Low physical activity (%)	29.8	48.5

Variables are expressed as percentage or mean ± SEM

Table 2 Pearson correlation coefficients between variables associated with MetS

	Waist circumference	HOMA-IR	TG	HDL-C	TG/HDL-C	SBP	Leptin
Men							
HOMA-IR	0.23**						
TG	0.34**	0.24**					
HDL-C	−0.10**	−0.06	−0.38**				
TG/HDL-C	0.31**	0.22**	0.92**	−0.58**			
SBP	0.34**	0.12**	0.17**	−0.05	0.14**		
Leptin	0.42**	0.27**	0.33**	−0.08*	0.28**	0.14*	
TPA	−0.25**	−0.28**	−0.11**	0.15*	−0.12**	−0.10*	−0.26**
Women							
HOMA-IR	0.20**						
TG	0.30**	0.22**					
HDL-C	−0.16**	−0.14**	−0.49**				
TG/HDL-C	0.28**	0.22**	0.91**	−0.71**			
SBP	0.36**	0.10**	0.17**	−0.03	0.15**		
Leptin	0.41**	0.18**	0.30**	−0.09*	0.26**	0.08*	
TPA	−0.26**	−0.26**	−0.12*	0.13*	−0.10*	−0.09*	−0.24**

* $P < 0.01$; ** $P < 0.001$

with SBP in both genders. There was no association between HDL-C and HOMA-IR in men. Discarding the correlation of TG/HDL-C ratio with its components (i.e., TG and HDL-C), in women the highest correlation coefficient was observed between TG and HDL-C. However, in men their correlation was just lower than the correlation between leptin and waist circumference.

Exploratory factor analysis

Entering conventional variables of Model 1 (i.e., waist circumference, HOMA-IR, TG, HDL-C, and SBP) as components of MetS, exploratory factor analysis extracted two factors with some differences in both genders (accounting for around 59.0% of the total variance in each gender, Table 3). TG and HDL-C were associated with the first and second extracted factors in women and men, respectively. Addition of leptin or TPA to the components of the MetS, alone or together with each other, led to a two-factor model, with leptin and TPA mainly loading on the first factor, in both genders.

Considering conventional variables of Model 2 (i.e., waist circumference, HOMA-IR, TG/HDL-C ratio, and SBP) exclusively or in together with leptin led to extraction of one factor in which waist circumference had the highest factor loadings (Table 4). An extra factor was identified when TPA was added to the variables of interest of Model 2.

ROC curve analysis revealed that addition of leptin increases the ability of the factor-based logistic regression scores in prediction of obesity (Table 5). The AUCs of Model 2 for diagnosis of women with high LDL-C levels were slightly lower than Model 1. The addition of TPA preceded increase in the ability of suggested models to detect subjects with low physical activity.

Discussion

Factor analysis extracted 1 or 2 factors depending on whether TG and HDL-C were considered as two distinct variables or were replaced by a composite measure. Modifying the models with leptin increased the ability of the models to identify obese subjects.

It has been demonstrated that using two or more measures for the same trait results in the extraction of more factors than really exist [14]. Similarly, our results show that TG and HDL-C tend to cluster together under a separate factor instead of loading on a common factor, maybe because among studied variables, the correlation coefficient between TG and HDL-C was among the highest coefficients. Therefore, when the two lipid alterations were replaced with a single composite variable, a single factor was sufficient to explain most of the variance in Iranian population, confirming previous studies on the monofactorial structure of MetS [14]. In this regard, AUCs of Models 1 and 2 for obesity and high LDL-C levels were not different except for detecting elevated LDL-C levels in women which were lower in Model 2 compared to Model 1. High LDL-C is significantly associated with MetS [20]. Since our study population is a representative sample of Iranian population we used cut-off point of LDL-C $\geq$ 160 mg/dl in our analysis [21]. TG, HDL-C, and LDL-C are all interrelated to each other; therefore, it is not unexpected to find

Table 3 Factor loadings of conventional variables (CV) of Model 1 with leptin and TPA on the selected factors

	CV1		CV1 + leptin		CV1 + TPA		CV1 + leptin and TPA	
	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2	Factor 1	Factor 2
Men								
Waist circumference	0.77*	0.19	0.78*	0.14	0.77*	−0.20	0.78*	0.14
HOMA-IR	0.50*	0.19	0.52*	0.16	0.49*	−0.21	0.51*	0.19
TG	0.34	0.77*	0.37	0.74*	0.32	−0.76*	0.36	0.73*
HDL-C	0.05	−0.87*	0.06	−0.87*	0.07	0.84*	0.06	−0.84*
SBP	0.77*	−0.11	0.66*	−0.15	0.78*	0.10	0.67*	−0.15
Leptin	–	–	0.64*	0.26	–	–	0.64*	0.26
TPA	–	–	–	–	−0.36	0.27	−0.41*	−0.30
% Variance explained	31.2	28.5	31.2	24.0	25.9	24.5	26.7	21.2
Women								
Waist circumference	0.25	0.70*	0.77*	0.18	0.43*	0.60*	0.78*	0.16
HOMA-IR	0.31	0.39	0.38	0.28	0.43*	0.21	0.41*	0.23
TG	0.79*	0.28	0.32	0.78*	0.82*	0.11	0.35	0.78*
HDL-C	−0.87*	0.03	0.05	−0.90*	−0.80*	0.17	0.03	−0.91*
SBP	−0.09	0.82*	0.59*	−0.04	0.17	0.71*	0.55*	0.15
Leptin	–	–	0.68*	0.15	–	–	0.71*	0.09
TPA	–	–	–	–	−0.43*	−0.25	−0.55*	−0.20
% Variance explained	31.3	27.8	27.8	25.9	29.5	20.2	24.3	21.7

Factors with an eigenvalue ≥1 were selected for analysis. CV1 refers to the conventional variables of Model 1 (i.e., waist circumference, HOMA-IR, TG, HDL-C, and SBP). HOMA-IR, TG, and leptin are log transformed

* Factor loadings ≥ |0.40|

Table 4 Factor loadings of conventional variables (CV) of Model 2 with leptin and TPA on the selected factors

	CV2	CV2 + leptin	CV2 + TPA		CV2 + leptin and TPA	
	Factor 1[a]	Factor 1[a]	Factor 1	Factor 2	Factor 1	Factor 2
Men						
Waist circumference	0.78*	0.77*	0.79*	−0.11	0.80*	0.04
HOMA-IR	0.57*	0.56*	0.45*	−0.39	0.50*	−0.31
TG/HDL-C	0.63*	0.60*	0.50*	−0.44*	0.53*	−0.40*
SBP	0.61*	0.51*	0.73*	0.17	0.21	−0.46*
Leptin	–	0.70*	–	–	0.68*	−0.15
Physical activity	–	–	−0.17	0.66*	−0.43*	0.20
% Variance explained	42.6	40.6	32.4	22.4	33.3	17.9
Women						
Waist circumference	0.73*	0.76*	0.63*	−0.41*	0.55*	0.44*
HOMA-IR	0.57*	0.52*	0.56*	−0.27	0.53*	−0.17
TG/HDL-C	0.68*	0.65*	0.68*	−0.14	0.65*	−0.02
SBP	0.57*	0.46*	0.57*	0.21	0.23	0.51*
Leptin	–	0.67*	–	–	0.68*	−0.03
Physical activity	–	–	−0.20	0.59*	−0.44*	−0.25
% Variance explained	40.9	38.4	32.7	20.5	31.8	17.3

Factors with an eigenvalue ≥ 1 were selected for analysis. CV2 refers to the conventional variables of Model 2 (i.e., waist circumference, HOMA-IR, TG/HDL-C, ratio and SBP). HOMA-IR, TG/HDL-C ratio, and leptin are log transformed

[a] Factor loadings are calculated without varimax rotation of variables

* Factor loadings ≥ |0.40|

Table 5 AUC (95% confidence interval) of suggested models for recognition of individuals with obesity, high LDL-C, and low physical activity

	Model 1				Model 2			
	CV1	CV1 + leptin	CV1 + TPA	CV1 +leptin and TPA	CV2	CV2 + leptin	CV2 +TPA	CV2 +leptin and TPA
Men								
BMI ≥ 30 kg/m^2	0.843 (0.816–0.870)*	0.864 (0.840–0.889)*†	0.844 (0.817–0.870)*	8.866 (0.841–0.890)*†	0.837 (0.810–0.864)*	0.857 (0.831–0.882)*†	0.841 (0.814–0.868)*†	0.862 (0.836–0.887)*†
LDL-C ≥ 160 mg/dl	0.646 (0.609–0.683)*	0.651 (0.613–0.689)*	0.643 (0.605–0.680)*	0.648 (0.611–0.686)*	0.636 (0.598–0.673)*	0.643 (0.605–0.681)*	0.632 (0.595–0.670)*	0.641 (0.603–0.679)*
Low physical activity	0.545 (0.511–0.580)*	0.548 (0.514–0.583)*	0.592 (0.559–0.625)*†	0.594 (0.561–0.626)*†	0.547 (0.512–0.581)*	0.550 (0.515–0.584)*	0.769 (0.744–0.795)*†‡	0.751 (0.724–0.777)*†‡
Women								
BMI ≥ 30 kg/m^2	0.798 (0.774–0.822)*	0.847 (0.826–0.869)*†	0.799 (0.775–0.823)*	0.850 (0.829–0.871)*†	0.798 (0.774–0.822)*	0.835 (0.812–0.857)*†‡	0.803 (0.779–0.827)*	0.839 (0.817–0.861)*†‡
LDL-C ≥ 160 mg/dl	0.660 (0.628–0.691)*	0.666 (0.635–0.698)*	0.658 (0.626–0.689)*	0.667 (0.636–0.698)*	0.654 (0.622–0.685)*‡	0.659 (0.628–0.691)*‡	0.653 (0.622–0.685)*‡	0.660 (0.628–0.691)*‡
Low physical activity	0.561 (0.539–0.583)*	0.566 (0.544–0.589)*	0.659 (0.630–0.688)*†	0.847 (0.827–0.867)*†	0.562 (0.539–0.584)*	0.565 (0.542–0.587)*	0.831 (0.810–0.853)*†‡	0.823 (0.801–0.845)*†‡

CV1 and CV2 refer to the conventional variables of Model 1 (i.e. waist circumference, HOMA, TG, HDL-C, and SBP) and Model 2 (i.e., waist circumference, HOMA, TG/HDL-C, and SBP), respectively

* $P < 0.01$ for diagnosis of selected features. † $P < 0.01$ compared to the similar model without inclusion of leptin and TPA. ‡ $P < 0.01$ compared to the Model 1 with the same additional variables

higher AUCs for detecting high LDL-C levels in a model which comprises both TG and HDL-C levels. However, TG/HDL-C ratio is suggested to be a reliable index in predicting insulin resistance [22] and coronary artery disease [23]. In a multivariable-adjusted logistic regression analysis, on the contrary to HDL-C, TG/HDL-C ratio was revealed to be associated with number of MetS components and HOMA-IR by sex strata in both participants with and without MetS [24]. Thus, it is conceivable to use TG/HDL-C ratio instead of TG and HDL-C in factor analysis of MetS especially in men.

As mentioned earlier, the plasma concentrations of leptin are directly related to body fat content [15]. Hyperleptinemia also reflects leptin resistance that is commonly present in obesity [25]. Leptin signaling may play an important role in regulating food intake and energy expenditure [15, 25]. In our study, leptin had the highest correlation with waist circumference which seems plausible because high waist circumference reflects high body fat content. Several large population-based studies have suggested strong positive association between leptin and MetS [26, 27]. As mentioned by others, redundant measures representing the same components of MetS should be omitted in factor analysis. This point can be achieved by using multiple regression analysis. Leptin was identified as an independent predictive marker of MetS after adjusting for potential confounding variables including BMI, HOMA-IR, and age (data not shown). Review of previous studies that have investigated clustering of leptin with components of MetS shows that leptin along with measures of obesity and insulin resistance usually loads on the first extracted factor [2, 3, 5], which is consistent with our findings. Further, we showed that the models which include leptin measures as a component of interest can diagnose obese subjects more accurately. Therefore, increment in leptin levels is a manifestation of the same pathophysiologic mechanism that underlies MetS and inclusion of serum leptin concentration as a component of MetS does not interfere with the monofactorial structure of MetS.

It has been suggested that insulin resistance is a common unifying theme that weaves together much of the components of MetS [8]. Leptin is associated with insulin resistance independent of waist circumference [28]. A number of mechanisms may directly link leptin to insulin resistance. For instance, impaired leptin action causes ectopic accumulation of TG in non-adipose tissue organs such as skeletal muscles, which per se enhances insulin resistance [25]. Plasma insulin concentrations have been reported as significant positive predictors of plasma leptin concentrations [3]. In this respect, prolonged insulin infusions cause slight elevations in plasma leptin levels [29]. Leptin is a risk marker for coronary events and hemorrhagic stroke [30,

31]. In a 5-year follow-up study, leptin was found as an independent predictive factor for the incidence of coronary heart disease [31]. Moreover, leptin is regarded as a factor which links obesity, MetS, and cardiovascular disorders [16]. Pladevall et al. [14] have found that the expanded one-factor model of MetS, which includes leptin and uric acid, is also plausible. Therefore, we suggest that leptin as a component of MetS deserves special consideration.

We also found that physical activity is associated with components of MetS (Table 2). Exercise training has been shown to decrease visceral fat accumulation, improve insulin sensitivity, increase HDL-C, decrease triglycerides (TG) levels, and decrease blood pressure independent of weight loss, although the aforementioned favorable effects of physical activity are stronger if associated with weight loss [6]. In a population-based sample those who engaged in a moderate- or high-intensity leisure-time physical activity for less than 1 h/week was 60% more likely to have MetS than those who spent at least 3 h/week in such physical activity [32]. Few studies have performed factor analysis on components of MetS and physical activity, but variations in variables analyzed and in methods used in interpretation preclude formal direct comparison [13, 32, 33]. Lakka et al. [32] have found that measures of cardiorespiratory fitness and physical activity along with most of the components of MetS cluster under a single factor, suggesting that a sedentary lifestyle and poor cardiorespiratory fitness are not only associated with MetS, but can also be considered as features of MetS. However, in two other studies physical activity loaded separately from components of MetS [13, 33]. In this study, although the addition of TPA was not consistent with the one-factor structure of MetS, generally it was associated with the first extracted factor which reflects the main underlying pathophysiologic mechanism of MetS.

It has been demonstrated that SBP in comparison to mean arterial pressure better predicts cardiovascular disease in men with different ages [34]. Therefore, it is conceivable to use SBP instead of mean arterial pressure especially when the age range of the population is wide.

The major strength of this study is that we used a large representative sample of Iranian population and performed the analysis in men and women separately. We also used a widely accepted reliable summary measure for physical activity that incorporated both intensity and duration. However, this study has also some limitations. Consistent with our analysis most previous studies have used cross-sectional study design to evaluate the interrelatedness of MetS components. The cross-sectional studies cannot determine the direction of causality for the relationship between different features of MetS. Therefore, longitudinal studies are suggested to better improve our understanding of MetS.

In conclusion, this study revealed that the concept of one underlying factor for the expression of MetS is plausible. The combination of two lipid alterations of MetS allows obtaining a single-factor structure which is maintained if leptin is also added among the components of MetS. Leptin is mediated by the pathophysiologic pathway that underlies core components of MetS. Thus, it is reasonable to suggest that regulating the level of leptin may influence the underlying pathway and subsequently lead to improvement of MetS. We also showed that addition of leptin increases the ability to diagnose obesity which is well reported to be associated with increased risk of coronary artery disease and diabetes [35, 36]. Further investigations are needed to determine which subjects with MetS can benefit the most from leptin adjustment and whether adding leptin to the definition improves the prognostic ability and predictive power of MetS for the development of coronary artery disease and diabetes. Further, this study revealed that although physical activity is not consistent with one-factor structure, it loads on the main identified factor. However, the role of the underlying pathophysiologic pathway of MetS in the impact of physical activity on individual MetS components remains to be fully elucidated.

Methods

Participants

Data of the third national surveillance of risk factors of non-communicable diseases (SuRFNCD-2007) in Iran were used in this study. Details of the survey have been reported previously [37]. In brief, a cluster sampling scheme was applied to randomly select a total number of 4,233 individuals as a representative sample of 25–64 years-old Iranian adults. The data were obtained and recorded in standardized questionnaires by trained health-care professionals in line with WHO recommendations. After excluding pregnant women, individuals with self-reported diabetes and individuals with missing data, analyses were performed on the remaining 3,001 subjects. The survey received ethics approval from the Center for Disease Control (CDC) of Iran and all participants gave verbal informed consent before study commencement.

Procedures and definitions

Weight and height of participants were determined in light clothing and without shoes. Waist circumference was measured at the end of a normal expiration with arms relaxed at the sides, at mid-distance between iliac crest and rib cage on the mid-axillary line and was rounded to the nearest 0.1 cm. The participants were instructed to rest for

at least 5 min before having their blood pressure checked thrice for at least 5 min intervals. The mean value of these three measurements was used for the analyses. Venous blood samples were collected following 12 h overnight fast. Fasting plasma glucose was measured by glucose oxidize test (intra- and inter-assay coefficients of variation less than 2.1 and 2.6, respectively). TG, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were determined by enzymatic methods (Parsazmun, Karaj, Iran). Insulin was measured by radioimmunoassay, using an antibody with no cross reaction against pro-insulin and C-peptide (Immunotech, Prague, Czech Republic). The intra- and inter-assay coefficients of variation were lower than 4.3 and 3.4, respectively. Serum leptin concentration was determined by an enzyme-linked immunosorbent assay (DRG Instruments GmbH, Germany) with an intra-assay coefficient of variation of 5.9–6.9% and an inter-assay coefficient of variation of 8.6–11.5%.

The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as fasting insulin (U/l) × fasting plasma glucose (mg/dl)/405, as described by Matthews et al. [38]. Body mass index (BMI) was defined as weight (kg)/height $(m)^2$ and subjects with BMI $\geq$ 30 kg/m^2 were diagnosed as having obesity.

Physical activity assessment

Physical activity was assessed according to the second version of global physical activity questionnaire (GPAQ). This questionnaire, which has been developed by WHO, is composed of 16 questions about physical activity in a typical week and measures physical activity in three domains as follows: work, transportation, and recreational activities. It also determines the intensity of activity (i.e., vigorous or moderate) in each domain as well as the time spent on sedentary behaviors such as watching TV. Sedentary behavior was defined as activities such as sitting at a desk, traveling in car/bus/train, reading, working with computer, and watching television. For determining energy expenditure, the concept of metabolic equivalents (MET) was used. MET is a value assigned to each activity showing the ratio of the corresponding activity metabolic rate relative to the resting metabolic rate. In GPAQ data, four METs are assigned to the time spent on moderate activities and eight MetS to the time spent on vigorous activities. The TPA score was calculated as the sum of all MET × minutes for moderate- or vigorous-intensity physical activities performed in work, transportation, and recreation per week.

Participants who did not fulfill the following conditions were classified in the category of low physical activity: three or more days of vigorous-intensity activity of at least 20 min/day, five or more days of moderate-intensity activity or walking of at least 30 min/day, or five or more days of any combination of walking, moderate-, or vigorous-intensity activities achieving a minimum of at least 600 MET-minutes per week.

Statistical analysis

Sex-specific analysis of data was performed using SPSS software (version 16.0; SPSS Inc., Chicago, USA). Data were weighted for sex, age, and residential area (urban/rural) strata, according to the population of Iran (national census, 2006). Complex sample survey analysis was performed based on the clusters of sampling protocol, strata (age groups, sex, and residential area), and the determined weights. National estimates, made in the complex survey analysis mode, are expressed as mean ± SEM. In order to improve the normality of skewed variables (i.e., TG, TG to HDL-C ratio [TG/HDL-C], HOMA-IR, and leptin) natural log transformations were used, as appropriate. The relationship between individual variables was examined using bivariate Pearson's correlation coefficients. Since a large number of analyses were carried out, a $P < 0.01$ was considered statistically significant. We performed our analyses in two separate models. In Model 1, exploratory factor analysis was performed on waist circumference, HOMA-IR, TG, HDL-C, and SBP using the method of principal component analysis, a technique for reducing the number of original variables into fewer latent factors. Factors with an eigenvalue (the amount of variance attributable to the factor) of greater than one were extracted and transformed by varimax rotation method to enhance interpretation. Varimax rotation cannot be performed if factor analysis extracts just one factor. In accordance with several previous reports [2–4, 11–13], factor loadings of $\geq|0.40|$ were considered meaningful for interpretation; because this ensures that the variable shares at least 15% of the variance with the factor [39]. Factor scores, which are estimates of individual factors with the mean and standard deviation equal to 0 and 1, respectively, were determined by regression method. Considering that two of the variables entered in analyses are related to lipid profile (i.e., TG and HDL-C) and highly correlated, in Model 2 we repeated aforementioned analyses substituting TG/HDL-C ratio for both TG and HDL-C.

Later we added leptin and TPA to the components of MetS individually or in together and repeated factor analysis. Further in each step factor scores were modeled using multiple logistic regression analysis in which different MetS-related features were regarded as dependent variables. Through receiver-operator characteristics (ROC) curve analysis, we evaluated how adding leptin and TPA to the components of MetS affects the ability of the factor-based logistic regression scores to identify subjects with

other features related to MetS. The following features were considered:

1. Obesity
2. Low physical activity
3. LDL-C $\geq$ 160 mg/dl

Area under the ROC curves were compared by STATA software (version 9.0, 2005).

Conflict of interest statement The authors declare no conflicts of interests.

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