

Is persistence of metabolic syndrome associated with poor health-related quality of life in non-diabetic Iranian adults? Tehran Lipid and Glucose Study

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Keywords

Metabolic syndrome, Persistency, Quality of life

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J Diabetes Invest 2014; 5: 687–693

doi: 10.1111/jdi.12222

ABSTRACT

Aims/Introduction: Previous research showed the association between health-related quality of life and metabolic syndrome (MetS). The present study aimed to examine the impact of persistence of MetS on health-related quality of life in non-diabetic Iranian adults.

Materials and Methods: This was a cross-sectional study. A representative sample of 643 non-diabetic individuals (67% female), aged ≥ 20 years, who participated in the Tehran Lipid and Glucose Study in 2005–2007 were recruited for the study, and categorized into four groups, those without, with transient, with intermittent and with persistent MetS. Health-related quality of life was assessed using the Iranian version of the Short Form Health Survey. MetS was diagnosed using the Joint Interim Statement criteria.

Results: Women with transient, intermittent and persistent MetS scored lower on the Physical Component Summary than those without the syndrome (51.03 ± 1.41 , 48.16 ± 1.46 and 46.58 ± 1.29 vs 52.18 ± 1.20) after adjusting for potential confounders ($P = 0.04$). In women, there was also a significant decreasing trend in the scores of bodily pain (P for trend = 0.006) and general health (P for trend = 0.005) across the study groups. Compared with women without MetS, the odds ratio of reporting poor health-related quality of life for women with intermittent MetS was 2.75 (95% confidence interval 1.19–6.37, $P = 0.01$). Among men, however, no significant difference was observed in any of the health-related quality of life domains.

Conclusions: Compared with women without, with transient and with persistent MetS, those with intermittent MetS reported poorer physical health-related quality of life.

INTRODUCTION

Metabolic syndrome (MetS) is defined as a cluster of metabolic disturbances, including central obesity, hyperglycemia, dyslipidemia and hypertension¹. It is evident that people with MetS are at increased risk for diabetes and cardiovascular disease^{2,3}. Both the unadjusted and the age-adjusted prevalences of MetS increased from National Health and Nutrition Examination Survey (NHANES) III to NHANES 1999–2006, respectively,

in USA adults⁴. The age standardized prevalence of MetS in an Iranian population according to the Adult Treatment Panel III, Adult Treatment Panel III/American Heart Association/National Heart, Lung and Blood Institute, and International Diabetes Federation criteria are 35.6%, 42.3% and 37.4%, respectively⁵, all considerably high.

Health-related quality of life (HRQoL) is an important marker of disease burden⁶, and is commonly used to evaluate a patient's subjective sense of physical and mental functioning, and well-being⁷. During the past two decades, for patients with

Received 18 December 2012; revised 11 January 2014; accepted 19 January 2014

chronic diseases, the HRQoL has become an important outcome of care given⁸. Considering the World Health Organization definition of health; that is, “state of complete physical, mental, and social well-being, and not merely the absence of disease and infirmity”, healthcare for patients with chronic diseases is care aimed at not only delaying death, but also at promoting health and quality of life^{9–11}.

As MetS is considered to be a chronic condition, in recent years, more attention has been paid to the assessment of the impact of MetS on HRQoL^{12–15}. In the context of a large population-based study carried out on non-diabetic subjects, we recently reported the impact of MetS on HRQoL in women, but not in men¹⁶. Although longer durations of cardiovascular risk factors, such as overweight, increase the risk of cardiovascular outcomes¹⁷, and also the long-term persistence of metabolic disorders can cause susceptibility to specific complications¹⁸, it seems reasonable to hypothesize that people with persistent MetS are more likely to report poorer HRQoL. Given the lack of data clarifying the manner in which people with varying persistency of MetS perceive their quality of life, in the present study, we examined the impact of persistence of MetS on the HRQoL in a large sample of non-diabetic Tehranian adults, over a duration of 6.7 years.

MATERIALS AND METHODS

Study Sample and Design

The present cross-sectional study was carried out between 2005 and 2007 on a population of the Tehran Lipid and Glucose Study (TLGS). The Tehran Lipid and Glucose Study, designed to determine risk factors for atherosclerosis in an urban population in Tehran, aims at developing population-based measures with the goal of changing lifestyles and halting the increasing trend of diabetes and dyslipidemia. The study was divided into two phases: (i) a cross-sectional study of the prevalence of non-communicable diseases, such as diabetes and cardiovascular disease, and their associated risk factors; and (ii) a prospective 20-year follow-up study. A multistage, stratified, cluster, random sampling technique was used to select 15,005 people, aged 3 years and older, from the urban district 13 of Tehran, the capital of Iran; this district is located in the center of Tehran, and the age distribution of its population is representative of the overall population of Tehran.

During sampling, a list of all households under the coverage of the district's three healthcare centers (the official bodies responsible for vaccination programs and collection of health-related statistics in a district) was used. Then, a random sample of households, stratified according to healthcare centers to achieve a distribution similar to the original population, was chosen, and from each household, all members, above the age of 3 years were recruited. The cross-sectional phase of TLGS began in 1997, and was completed in 2000; the first follow-up survey began in 2001, was completed in 2004 and surveys are being repeated every 3 years^{19,20}.

This was a second data analysis carried out in the framework of the TLGS. According to the original study, TLGS population

is a representative sample of the urban population of Tehran, the capital of Iran. From 12,521 individuals participating in TLGS between September 2005 and September 2007, a sample of 1,255 individuals aged 20 years and older, including those who were diagnosed as having MetS, and an age- and sex-matched control group were recruited. All the participants were interviewed by a trained interviewer to obtain data on HRQoL, sociodemographics, physical activity, smoking habits and medications used. From the initial sample, 275 (21.9%) participants were diagnosed as diabetic and excluded from the study. After further exclusion of 30 (3.1%) participants with missing data, the information of 950 participants was considered as complete data.

For the current study, the data of 643 (67.7%) participants, who had participated in all three phases of TLGS (the initial cross-sectional survey and two follow ups), were analyzed (Figure 1). The participants were categorized into four groups: (i) without MetS in all three phases; (ii) transient (those with MetS for just one phase); (iii) intermittent (those with MetS for 2 continuous or intermittent phases); and (iv) persistent (those with MetS for all three phases; Table 1).

All participants gave written informed consent. The study was approved by the ethics committee of the Obesity Research Center, Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

Quality of Life Measure

Health-related quality of life was measured using the Iranian version of the Short Form Health Survey (SF-36), a widely used questionnaire measuring eight health-related concepts including, physical functioning, role limitations as a result of physical problems, bodily pain, general health, vitality, social functioning, role limitations as a result of emotional problems and mental health, as well as a summary of physical and mental measures²¹. The psychometric properties of the Iranian version of SF-36 are well documented²². For each scale, scores ranged from 0 (the worst) to 100 (the best).

Definitions

MetS was defined according to the Joint Interim Statement²³ as the presence of any three of the following five risk factors: (i) abdominal obesity as waist circumference (WC) ≥ 95 cm for both sexes based on the guidelines of the Iranian National Committee for Obesity^{5,24}; (ii) fasting plasma glucose (FPG) ≥ 5.6 mmol/L or drug treatment; (iii) fasting triglycerides (TG) ≥ 1.7 mmol/L or drug treatment; (iv) fasting high-density lipoprotein cholesterol (HDL-C) < 1.03 mmol/L in men and < 1.3 mmol/L in women or drug treatment and (v) raised blood pressure defined as systolic blood pressure (SBP) ≥ 130 mmHg, diastolic blood pressure (DBP) ≥ 85 mmHg or antihypertensive drug treatment.

Additional Measures

Waist circumferences were measured initially at baseline and again at each follow-up phase, at the umbilical level, over light

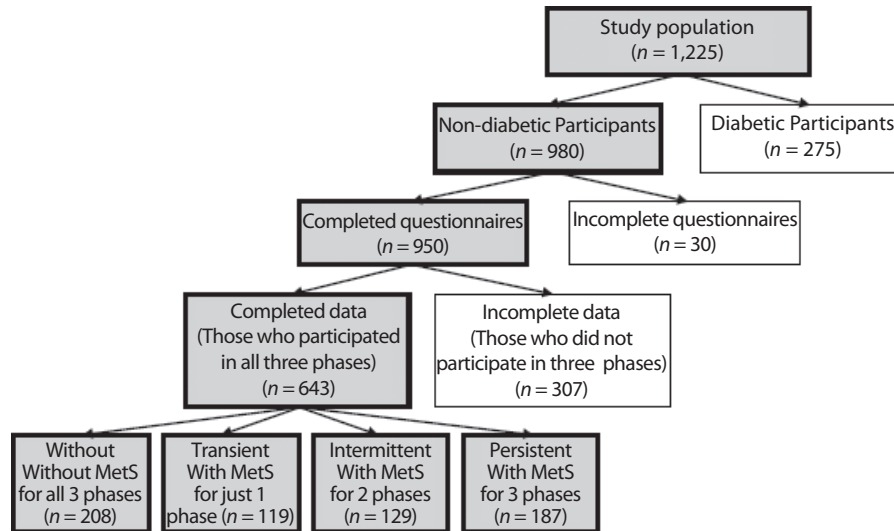


Figure 1 | The sampling frame of the study.

Table 1 | Definition of study groups based on metabolic syndrome status in three phases of the Tehran Lipid and Glucose Study

Study groups	Phase III (2005–2008)	Phase II (2001–2004)	Phase I (1997–2000)
Metabolic syndrome status			
Persistent (n = 187)	+	+	+
Intermittent (n = 129)	+	–	+
Transient (n = 119)	–	+	+
Without (n = 208)	–	–	–

Intermittent, those with metabolic syndrome for two phases; Persistent, those with metabolic syndrome for all three phases; Transient, those with metabolic syndrome in just one phase; Without, those without metabolic syndrome in all three phases.

clothing, using an unstretched tape meter, without any pressure to body surface and measurements were recorded to the nearest 0.1 cm. Blood pressure was measured twice, after participants were seated for 15 min, using a standard mercury sphygmomanometer. There was at least a 30-s interval between these two separate measurements, and the mean of two measurements was considered the patient’s blood pressure. Then, 12-h fasting blood samples were collected in tubes containing 0.1% ethylenediaminetetraacetic acid, and were centrifuged at 4°C and 500 g for 10 min to separate the plasma. Blood glucose was measured on the day of blood collection by an enzymatic colorimetric method using glucose oxidase. Serum total cholesterol and triglyceride concentrations were measured with commercially available enzymatic reagents (Pars Azmoon, Tehran,

Iran) adapted to a selectra autoanalyzer. HDL-C was measured after precipitation of the apolipoprotein B-containing lipoproteins with phosphotungstic acid. Low-density lipoprotein cholesterol was calculated from serum total cholesterol, TG and HDL-C, except when TG concentration was >4.56 mmol/L. Additional information on age, smoking status (considered in two groups: group 1, non- and ex-smokers; and group 2, current smokers), physical activity, and current use of oral hypoglycemic agents, lipid lowering and antihypertensive medication, were obtained from the TLGS data already documented.

Statistical Analysis

Continuous and categorical data are presented as means ± standard error and percentages, respectively. Categorical variables were compared using the χ^2 -test. Health-related quality of life scores among the four study groups were compared using ANCOVA, and the independent effect of persistency of MetS was assessed using multiple logistic regression analysis, controlled for the effects of age, marital status, education level, medication, and the presence of MetS at the time of the test (phase III) in men and women separately. For the purpose of logistic regression analysis, the Physical Component Summary (PCS) and Mental Component Summary (MCS) were used, and relative to the mean scores, the study sample was divided into two groups: (i) those who scored equal or greater than the mean; and (ii) those who scored below it. Analysis was carried out using SPSS software version 15.0 (SPSS, Chicago, IL, USA).

RESULTS

The general characteristics of participants are listed in Table 2. The mean ages of the all participants were 43.65 ± 14.5, 47.47 ± 13.66, 52.24 ± 13.51 and 54.05 ± 11.70 years for those without, with transient, with intermittent and with persistent MetS, respectively (P < 0.001). In those with persistent MetS,

Table 2 | General characteristics of the study sample

	Women (n = 431)				Men (n = 212)			
	Without (n = 155)	Transient (n = 85)	Intermittent (n = 71)	Persistent (n = 120)	Without (n = 53)	Transient (n = 34)	Intermittent (n = 58)	Persistent (n = 67)
Age, years (mean ± SD)	42.19 (13.70)*	46.24 (12.81)	53.17 (10.98)	55.47 (11.02)	47.96 (10.08)	50.56 (13.38)	51.10 (16.11)	51.52 (12.53)
Marital status								
Married	136 (87.7)*	82 (96.5)	71 (100.0)	120 (100.0)	43 (81.1)*	32 (94.1)	50 (86.2)	66 (98.5)
Educational level								
Primary	56 (37.6)*	35 (43.2)	41 (64.1)	67 (67.0)	18 (34.0)	10 (29.4)	22 (38.6)	20 (30.8)
Secondary	65 (43.6)	35 (43.2)	20 (31.3)	30 (30.0)	22 (41.5)	16 (47.1)	21 (36.8)	28 (43.1)
Higher	28 (18.8)	11 (13.6)	3 (4.7)	3 (3.0)	13 (24.5)	8 (23.5)	14 (24.6)	17 (26.2)
Physical activity (MET h/week) (Mean ± SD)	9.96 (15.92)	10.19 (14.66)	10.25 (15.04)	10.37 (18.12)	10.09 (16.64)	18.81 (32.91)	16.93 (25.64)	18.17 (33.74)
Smoking								
Daily/occasionally	1 (0.6)	1 (1.2)	2 (2.9)	2 (1.7)	11 (20.8)	6 (17.6)	9 (15.5)	12 (17.9)
Ex-smoker/never smoked	154 (99.4)	84 (98.8)	66 (97.1)	114 (98.3)	42 (79.2)	28 (82.4)	49 (84.50)	55 (82.1)
Medication†								
User	4 (2.6)*	5 (6.0)	11 (15.9)	29 (25.9)	1 (1.9)	1 (2.9)	4 (7.0)	5 (7.6)

Data are presented as n (%) unless stated otherwise. * $P < 0.001$. †Individuals who were taking hypertensive or anti lipid drugs. Intermittent, those with metabolic syndrome for two phases; Persistent, those with metabolic syndrome for all three phases; Transient, those with metabolic syndrome in just one phase; Without, those without metabolic syndrome in all three phases. MET, Metabolic Equivalent Task; SD, standard deviation.

married status, primary level of education and medication use were more prevalent compared with the other three groups. However, no significant differences were seen in the frequency of smoking and mean values of weekly physical activity among study groups.

For the individual components of MetS, women and men with persistent MetS had the highest waist circumference compared with those in the without, with transient and with intermittent MetS groups ($P < 0.001$). After adjusting for potential confounders, the highest levels of TG ($P < 0.001$), FBS ($P < 0.001$), SBP ($P < 0.001$), DBP ($P < 0.001$) and the

lowest level of HDL-C ($P < 0.001$) were also found for those with persistent MetS in both sexes (Table 3).

Sex-specific analysis of SF-36 subscales showed that in women, after adjustment for potential confounders, there were significant differences in the mean scores of bodily pain ($P < 0.05$), and general health ($P < 0.05$) among study groups (Table 4). Compared with the other three study groups, the lowest PCS scores were also seen in women with persistent MetS as follows: persistent MetS 46.58 ± 1.29 vs intermittent MetS 48.16 ± 1.46 vs transient MetS 51.03 ± 1.41 vs without MetS 52.18 ± 1.20 ($P < 0.05$; Figure 2). However, in men, no

Table 3 | Metabolic syndrome components among study groups by sex

	Women (n = 431)				Men (n = 212)			
	Without	Transient	Intermittent	Persistent	Without	Transient	Intermittent	Persistent
Waist circumference (cm)	79.4 ± 1.4	87.6 ± 1.6	92.6 ± 1.7	93.3 ± 1.5	85.0 ± 1.9	91.6 ± 2.2	97.2 ± 1.8	104 ± 1.9
Triglycerides (mmol/L)	1.2 ± 0.1	1.6 ± 0.2	2.0 ± 0.2	2.3 ± 0.1	1.0 ± 0.2	1.3 ± 0.3	1.9 ± 0.2	2.5 ± 0.2
Fasting blood sugar (mmol/L)	4.7 ± 0.06	5.0 ± 0.07	5.0 ± 0.08	5.2 ± 0.07	4.8 ± 0.1	5.1 ± 0.1	5.1 ± 0.1	5.3 ± 0.1
High-density lipoprotein (mmol/L)	1.4 ± 0.04	1.2 ± 0.04	1.1 ± 0.04	1.0 ± 0.04	1.2 ± 0.04	1.0 ± 0.04	1.0 ± 0.04	0.9 ± 0.04
Systolic blood pressure (mm/hg)	110 ± 2.1	114 ± 2.5	117 ± 2.6	127 ± 2.3	120 ± 3.5	122 ± 4.0	129 ± 3.3	130 ± 3.5
Diastolic blood pressure (mm/hg)	68.4 ± 1.3	71.4 ± 1.6	73.6 ± 1.6	76.7 ± 1.4	72.5 ± 2.2	75.6 ± 2.5	77.1 ± 2.1	80.4 ± 2.2

Data are presented as mean ± standard error, adjusted for age, marital status, education level and medication use. Data are significant at $P < 0.001$ for all metabolic syndrome components among study groups in both sexes. Intermittent, those with metabolic syndrome for two phases; Persistent, those with metabolic syndrome for all three phases; Transient, those with metabolic syndrome in just one phase; Without, those without metabolic syndrome in all three phases.

Table 4 | Short Form Health Survey scores according to metabolic syndrome status in study groups by sex

	Women (n = 431)				Men (n = 212)			
	Without	Transient	Intermittent	Persistent	Without	Transient	Intermittent	Persistent
Physical functioning	81.11 ± 3.29	79.41 (3.88)	74.91 (4.00)	74.62 (3.54)	76.67 (4.65)	79.66 (5.35)	76.75 (4.51)	69.88 (4.72)
Role physical	72.72 (5.31)	69.05 (6.26)	66.63 (6.45)	68.85 (5.71)	57.56 (7.81)	68.76 (8.99)	61.03 (7.57)	67.48 (7.93)
Bodily pain	75.56 (2.96)	75.54 (3.50)	68.62 (3.60)	66.57 (3.19)*	70.48 (3.62)	74.04 (4.17)	71.36 (3.51)	70.79 (3.68)
General health	70.09 (2.71)	69.19 (3.19)	62.64 (3.29)	61.63 (2.91)*	62.08 (4.03)	64.84 (4.64)	60.24 (3.91)	60.58 (4.09)
Vitality	60.77 (3.14)	60.01 (3.71)	61.91 (3.82)	57.41 (3.38)	63.49 (4.41)	63.87 (5.08)	61.50 (4.28)	66.16 (4.48)
Social functioning	80.98 (3.57)	79.52 (4.21)	77.90 (4.33)	76.54 (3.83)	71.24 (4.88)	70.10 (5.62)	68.26 (4.73)	71.35 (4.96)
Role emotional	69.37 (5.92)	76.24 (6.99)	78.64 (7.20)	77.73 (6.37)	57.00 (8.74)	74.36 (10.06)	52.54 (8.48)	62.65 (8.88)
Mental health	67.12 (3.04)	67.09 (3.58)	66.11 (3.69)	62.69 (3.27)	70.71 (4.29)	70.59 (4.94)	65.80 (4.16)	70.56 (4.36)

Data are presented as mean ± standard error, adjusted for age, marital status, education level and medication use. **P* < 0.05 compared to without metabolic syndrome group. Intermittent, those with metabolic syndrome for two phases; Persistent, those with metabolic syndrome for all three phases; Transient, those with metabolic syndrome in just one phase; Without, those without metabolic syndrome in all three phases.

significant difference was seen in any of the SF-36 scales and subscales (Table 4).

Compared with men, in physical HRQoL, women with intermittent MetS showed higher odds ratios (ORs) for poor HRQoL before and after adjustment for confounding variables (*P* < 0.001); these ORs for the mental component summary scores were not significant for men and women, even after adjustment (Table 5).

DISCUSSION

The present study shows that after adjusting for potential confounders, women with persistent and intermittent MetS had lower physical HRQoL scores than those without the syndrome. Among men, however, no significant difference was observed in any of the HRQoL domains among the study groups. Furthermore, compared with women without MetS, those with intermittent MetS were more likely to report poor physical HRQoL, even after adjusting for potential confounders.

There have been numerous reports regarding the association between HRQoL and cardiometabolic risk factors, such as diabetes mellitus²⁵, hypertension²⁶ and obesity^{27,28}; however, none of these reports have investigated the impact of the mentioned risk factors on HRQoL over time. Furthermore, despite a number of studies having documented the association between HRQoL and MetS^{12–16}, to best of our knowledge this is the first report regarding the relationship between persistency of this syndrome and HRQoL.

People with MetS usually deal with several cardiometabolic risk factors, and the HRQoL in these individuals can vary in the long term. The results of the current study regarding the positive association between persistency of MetS and HRQoL in women confirm this hypothesis, and also reconfirm the prominent role of sex in the association mentioned during a 6.7-year investigation, a finding in line with our previous report that showed the effective role of sex in relation of HRQoL and MetS¹⁶. Although persistency of the syndrome was diversely associated with a deteriorating trend of its components in both

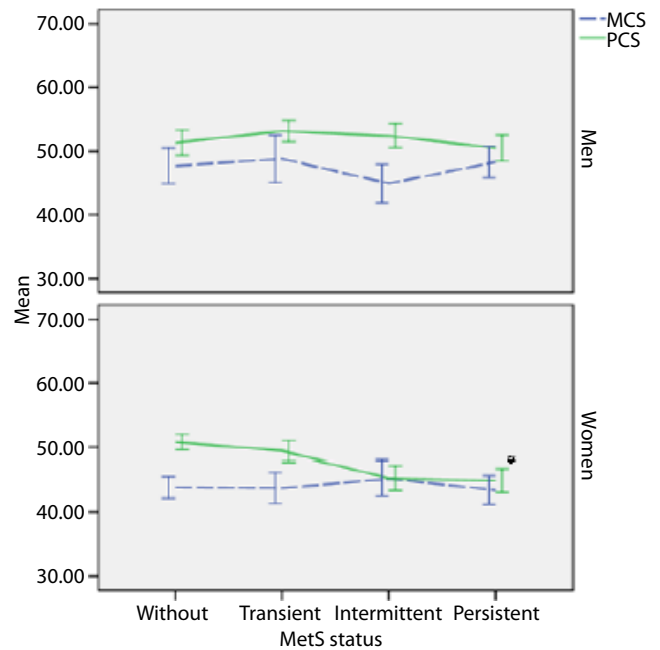


Figure 2 | Means of the physical and mental component summary scores among study groups in men and women. **P* < 0.001. Intermittent, those with metabolic syndrome for two phases; MCS, Mental Component Summary; MetS, metabolic syndrome; PCS, Physical Component Summary; Persistent, those with metabolic syndrome for all three phases; Transient, those with metabolic syndrome for just one phase; Without, those without metabolic syndrome in all three phases.

sexes, the association between persistency of MetS and HRQoL was seen only in women. This finding implicates the main role of sex differences regarding the aspect of interpretation of diseases more than their severity and duration, one possible reason for this could be different socially constructed roles for men and women, resulting from different social norms and expectations of society²⁹. It has been found that women experience

Table 5 | Results of multiple logistic regression analysis for poor health-related quality of life in men and women

	Women (n = 431) OR (95% CI)			Men (n = 212) OR (95% CI)		
	Transient	Intermittent	Persistent	Transient	Intermittent	Persistent
PCS						
Model 1	1.36 (0.77–2.38)	3.86 (2.14–6.96)*	3.20 (1.94–5.28)*	0.68 (0.24–1.70)	0.92 (0.43–1.95)	0.93 (0.45–1.94)
Model 2	1.17 (0.62–2.18)	2.75 (1.19–6.37)*	1.70 (0.64–4.50)	0.65 (0.25–1.96)	0.90 (0.33–2.47)	1.02 (0.30–3.60)
MCS						
Model 1	0.87 (0.51–1.48)	0.68 (0.38–1.20)	0.90 (0.56–1.46)	1.25 (0.51–3.03)	1.78 (0.83–3.83)	1.06 (0.50–2.25)
Model 2	0.75 (0.42–1.36)	0.60 (0.27–1.34)	0.68 (0.27–1.74)	1.02 (0.40–2.64)	0.98 (0.4–2.63)	0.37 (0.11–1.30)

Data are presented as Odds Ratio (95% CI), those without metabolic syndrome considered as reference group. PCS: Physical Component Summary, MCS: Mental Component Summary. Model 1. Unadjusted. Model 2. Adjusted for age, marital status, education level, medication use and presence of MetS in phase III. Without: Those without metabolic syndrome in all three phases; Transient: Those with metabolic syndrome in just one phase; Intermittent: Those with metabolic syndrome for two phases; Persistent: Those with metabolic syndrome for all three phases. * $P < 0.001$ compared to without metabolic syndrome group.

greater distress including mood and anxiety disorders than do men³⁰. Based on the two global hypotheses, this paradoxical sex difference could be explained by differences in exposure and vulnerability in men and women; the first one suggests that reduced access to materials and social conditions causes reporting of higher levels of health problems in women, whereas the second hypothesis refers to higher reactivity or responsiveness among women to life events and stressors, compared with men^{31,32}.

The present results show that in women, not in men, of the three study groups (second to fourth) that define different persistency of MetS, those who were placed in the intermittent group (third group) showed the largest ORs for poor PCS scores. Therefore, based on the present results, women with intermittent MetS reported poorer physical HRQoL compared not only with those without this syndrome, but also in women with the persistent and transient conditions of this syndrome. A possible reason for this finding could be that experiencing a chronic condition for a long time could result in adaptation to it, and lower the individual's sensitivity and responsiveness to that condition.

The main strength of the present survey is that we studied the impact of persistency of MetS on HRQoL in a large sample of non-diabetic adults in the general population. To the best of our knowledge, there is no previous report on the association between persistency of MetS and HRQoL. Thus, the findings of the present study could help to better understand the effect of the syndrome over time. However, some limitations of the present study deserve comment. First, our theoretical background of distributing participants in the three MetS groups (persistent, intermittent and transient) is yet a novel approach, and therefore complementary studies are recommended in these areas, especially to test this distribution with some other MetS definitions. Second, in those who had the syndrome for all three phases (persistent group) we did not have access to the date of onset of the syndrome, and we were hence unable to estimate the exact time of its duration.

Third, all participants with MetS for two phases (intermittent group) were considered and analyzed as one group, whereas all of them had different statuses of MetS in TLGS phases; at the time of reporting, some of the patients had MetS, whereas the others did not; however, the sample size limitation prevents us from analyzing these patients separately. Fourth, major depression was not evaluated. Last, but not the least, we gathered HRQoL data only in phase 3; it would better to have aforementioned data from all phases to show changes of HRQoL scores over time.

The results show that intermittent MetS is associated with poor physical HRQoL in women, but not in men, findings that show the prominent role of sex in the association between MetS status and HRQoL. Furthermore, the present results show that women, with intermittent MetS, reported poorer physical HRQoL than those with a persistent condition of this syndrome, possibly a result of adaptation to the chronic condition over time among the latter group.

ACKNOWLEDGMENTS

We appreciate the cooperation the participants of the Tehran Lipid and Glucose Study. We also acknowledge Ms Niloofar Shiva for critical editing of English grammar and syntax of this manuscript. All the authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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