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Longitudinal association of metabolic syndrome and dietary patterns: A 13-year prospective population-based cohort study

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KEYWORDS
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Abstract *Background and aims:* Diet is a potential factor contributing to the development of the Metabolic Syndrome (MetS). This longitudinal study with repeated measurements of dietary intake was thus conducted to examine the longitudinal association between major dietary patterns and risk of MetS.

Methods and results: The study was conducted within the framework of the Isfahan Cohort Study (ICS), in which 1387 participants were followed from 2001 to 2013. Validated food frequency questionnaire, anthropometric measurements, blood pressure, fasting serum lipids and blood sugars were evaluated in three phases of the study. Mixed effect Logistic and Cumulative Logit regressions were applied to evaluate the longitudinal associations between dietary patterns change and MetS and number of MetS components.

Three dietary patterns were identified: Healthy, Iranian and Western dietary patterns. After adjustment for potential confounders, the higher scores of Healthy diet were inversely associated with the risk of MetS and number of MetS components (OR: 0.50, 95% CI: 0.36–0.70, OR: 0.52, 95% CI: 0.39–0.70, respectively). The greater adherence to the Iranian diet was positively associated with the risk of MetS and number of MetS components (OR: 1.28, 95% CI: 1.01–1.65, OR: 1.45, 95% CI: 1.16–1.81, respectively). The Western dietary pattern did not show any significant associations.

Conclusion: Adherence to a Healthy diet was associated with lower risk of MetS even in a developing country setting. However, the Iranian diet was positively associated with the risk of MetS. These results may guide the development of improved preventive nutrition interventions in this adult population.

Abbreviations: ICS, Isfahan Cohort Study; ICRC, Isfahan Cardiovascular Research Center; SES, socioeconomic status; PCA, principle component factor analysis.

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Introduction

The Metabolic syndrome (MetS), as a cluster of metabolic risk factors, is considered as a major intermediate outcome of both cardiovascular diseases (CVD) and diabetes. When metabolic risk factors occur simultaneously, this increases the risk of incident CVD and diabetes and their associated morbidity and mortality [1]. Over the past decade, a high prevalence of MetS in the Iranian adult population has been reported [2,3]. The dietary patterns of the Iranian population have been changed as a result of nutrition transition phenomenon [4]. These changes along with other unhealthy lifestyle behaviors might contribute to an increased risk of MetS in Iranian adults [2,3].

Dietary patterns which focus on a combination of several foods can provide synergic effects rather than the effects described for individual nutrients or foods [5]. Some epidemiological studies have reported that certain dietary patterns characterized by high fruit, vegetable, whole grain, low-fat dairy intake and fish have a protective effect against MetS or its components [6–9], whereas dietary patterns characterized by high intake of red meat, processed meat, refined grains and fried foods were associated with increased risk of MetS [7,8,10,11]. However, there is inconsistency over a traditional dietary pattern in nutritional studies from the local population. Also, the subjects may not have complied to a diet for a sufficiently long time to prevent the condition. Thus, longitudinal observational studies with repeated measurements of dietary intake during the follow-up are needed to assess the ability of dietary patterns to prevent MetS.

To the best of our knowledge, there are limited longitudinal nutritional epidemiological studies with repeated measurements of dietary intake evaluating the association between dietary patterns and the risk of MetS [12–17]. Moreover, most of them focused on a Mediterranean type of diet [12–15] or on specific food groups [16]. In addition, they were mostly limited to baseline assessment of diet [12,15] or considered the average of repeated measurements of diet [13,14,16] instead of as a time-varying covariate. The ARIC study, a multicenter population-based prospective cohort study, assessed the relation between dietary patterns and incidence of MetS. Dietary covariates were modeled based on the mean of baseline diet and, six years later, examination diet [17]. Also, in all previously published studies, the number of MetS components was not considered and there is a lack of repeated measurement information on MetS.

Therefore, the novelty of this study is that it considers the repeated measurements of dietary intake as time-varying covariates and also the repeated measurement of outcome variable, to take into account the participants change during the long follow-up period (13 years). We applied the mixed regression analysis approach to construct models where repeated measurements of the pattern scores were inserted into the model so as to predict repeated measurements of the outcome variables; therefore, all models were longitudinal. Thus, the main aim of this study was to provide longitudinal evidence to identify the association of most frequent dietary patterns and the number of MetS components among an adult population in central Iran. Additionally, we further examined the longitudinal association between dietary patterns and the presence of MetS (yes/no).

Methods

Study population

This longitudinal study was conducted on 1387 subject who participated in all three phases of the Isfahan Cohort Study (ICS). The ICS is a population-based, longitudinal study of 6504 adults aged 35 years old or more recruited from urban and rural areas of three districts in central of Iran from January to September 2001. Participants were selected by multistage random sampling to reflect age, sex and urban/rural distribution of the community. Laboratory measurements, physical examinations, and interviews were conducted at baseline and repeated in those without any CVD events in 2007 and 2013. Among them, 1387 participants who underwent repeated measurements in both 2007 and 2013, with complete information on dietary intake, covariates, and outcome were included in the current study. The protocol used in the 2007 and 2013 survey was similar to what was used in 2001. Study design, details of subjects' recruitment and data collection methods have been described previously [18].

The study was approved by the Ethics Committee of Isfahan Cardiovascular Research Center (ICRC), a World Health Organization-collaborating center, and informed written consent was obtained from each participant individually.

Assessment of covariates

Detailed home interview in three phases of the study was carried out by trained health professionals based on a designed questionnaire to determine socioeconomic and demographic characteristics as well as lifestyle components including nutrition, smoking, and physical activity.

We quantified socioeconomic status based on factor analysis and divided the participants into tertiles according to their score. Occupation type, education level and income were used as inputs of the factor analysis. The number of people aged under 18 and over 65 and the number of those aged 18 to 65 at home were also added so as to consider the population that is economically dependent in the active age group. The occupation type was classified using the following categories: "upper white-collar employees", "lower white-collar employees", "manual workers", "self-employed persons", "unemployed", "retired", and "housewife" groups. We categorized education level as illiterate, primary school, guidance school, high school, associate or bachelor degree, and master's degree or higher. Income was categorized into five following groups, $<$5 million RIALs (Iranian currency unit), 5–9 million RIALs, 9–15 million RIALs, 15–20 million RIALs and $>$20 million RIALs. Individuals in the lowest tertile of the score were classified as a low SES; individuals in the second tertile were labeled as a medium SES, whereas those in the highest tertile were classified as a high SES.

Smoking status was categorized as smoker for those who smoked at least one cigarette per day at the time of the study; ex-smoker for those who had previously smoked at least one cigarette per day, and non-smoker.

The data on physical activity (PA), expressed as metabolic equivalent hours per week (MET-h/wk.), were obtained through the Iranian version of the International Physical Activity Questionnaire (IPAQ), whose reliability and validity have been confirmed in several studies [19–21]. In the study conducted by Kelishadi et al., a self-administered and interview-administered questionnaire was filled out. The coefficient correlation between two methods was estimated as 0.87. Also, significant inverse relationship was found between the mean daily PA with the mean weight ($r = -0.64$, $P < 0.001$), and with the mean body mass index ($r = -0.71$, $P < 0.001$). Findings of this study provided a valid self-report questionnaire [19]. Vasheghani-Farahani et al. applied a forward–backward translation procedure to develop the Persian version of the IPAQ. Their findings indicated that the questionnaire was received well and all domains met the minimum reliability standards (intra-class correlation [ICC] > 0.7), except for Leisure-time physical activity. Aerobic fitness showed a weak positive correlation with all of the PA results derived from the IPAQ. A significant correlation was observed between the IPAQ data for total PA and both aerobic fitness ($r = 0.33$, $P < 0.001$) and BMI ($r = -0.26$, $P < 0.001$) [20]. Moghaddam et al. used the procedure of forward–backward translation for scale translation and face validity. The construct validity of IPAQ was conducted using exploratory factor analysis (EFA) and Confirmatory factor analysis (CFA). Varimax rotation was used for factor analysis and five factors were defined for IPAQ. The values for Comparative Fit Index (CFI), Goodness of Fit Index (GFI) and the Adjusted GFI (AGFI) were 0.83, 0.93, and 0.86 respectively, indicating an acceptable fit to the data. The mean of Content Validity Index (CVI) and Content validity Ration (CVR) was 0.85 and 0.77 respectively indicating a good content validity for IPAQ. Cronbach's Alpha coefficient (0.7) showed a good internal consistency for this instrument. Spearman Brown correlation coefficient (0.9) showed a good test retest reliability [21]. Total physical activity was calculated based on four domains: leisure time, occupational, household, and transportation physical activities. We requested participants to report the above items in their everyday life as well as the time spent on these activities in each session and their frequency per week. To obtain total physical activity value, the amounts of physical activities in all items were added together.

Trained physicians conducted medical interviews and physical examinations. Blood pressure and anthropometric measurements were taken according to standard protocols. Fasting blood samples were taken and serum lipid profiles along with plasma glucose levels were quantified.

Dietary assessment

Repeated measurements of dietary intake data were obtained using a simplified 48-item food frequency questionnaire (SFFQ) by trained interviewers in a face-to-face manner [4,22]. The FFQ and the procedures used for completing and calculating dietary intake were repeated in the same way in three phases. Participants reported the frequency consumption of each food item during the previous year regarding daily, weekly and monthly consumption. All frequencies were converted to weekly consumption. Reported never or rarely consumed food items were scored as 'zero'. Food items were categorized in certain food groups (Table 1) based on similarity of nutrients [4]. Thus, we came up with 21 groups.

The validation study showed reasonably relative validity and reproducibility of SFFQ. The SFFQ was validated by comparing one 24-h dietary recall and two-day dietary record in 264 adults. Spearman correlation coefficient between examined and reference methods ranged from 0.105($P = 0.378$) to 0.48 ($P < 0.001$) and ICC for reproducibility of FFQ was between 0.47 and 0.69 ($P < 0.001$) in different food groups [22].

Metabolic syndrome criteria

The MetS was defined if the study participant had three or more defined criteria by the Adult Treatment Panel III of the National Cholesterol Education Program (ATP-III) [23]: (1) fasting triglycerides > 150 mg/dL or lipid medications; (2) SBP > 130 mmHg, DBP > 85 mmHg, or use of antihypertensive medications; (3) fasting plasma glucose > 110 mg/dL

Table 1 Food grouping used in the dietary pattern analyses.

Food groups	Food items
Whole dairy product	Whole fat milk, whole fat yogurt
Fast foods	sausages, hamburger, pizza
Animal fat	Ghee, butter, tallow
Organ meats	Liver, lung
Fruits and vegetables	Fresh fruits, fruit juices, dried fruits, raw vegetables, cooked vegetables, dried vegetables
Sweets	Pastry, biscuits, cookies, chocolates, jam
Red meat	Beef, lamb
Chicken	Chicken
Fish	Fish
Hydrogenated oil	Hydrogenated oil
Liquid oil	Liquid oil
Olive oil	Olive oil
Bread	All kind of bread
Rice	Rice
Pickles	Pickle and salty cucumber
Beans	Beans
Egg	Egg
Nuts	Almonds, pistachios, hazelnuts, roasted seeds, walnuts
Canned foods	All kind of canned food
Carbonated beverages	All kind of carbonated beverages
Fried foods	All kind of foods fried in oil

or use of diabetes medications; (4) HDL cholesterol < 40 mg/dL (men) or <50 mg/dL (women); and (5) waist circumference > 102 cm (men) or >88 cm (women).

In the current study, further evaluation of MetS according to the number of components (ordinal scale), in spite of evaluating the presence of MetS (yes/no) was done.

Statistical analysis

Owing to the lack of data on energy intake in the current study, we first used BMI as a surrogate measure to obtain energy-adjusted intakes of food groups for each study year [24,25]. Using the residual method of Willett [26], all dietary intakes of food groups were adjusted for BMI. Principal component factor analysis (PCA) was applied to identify major dietary patterns based on the BMI-adjusted food groups. PCA was performed separately for each study phase, and the factors were rotated by an orthogonal transformation. We focused on the interpretability of the factors, eigenvalues more than 1.5 and the Scree test to determine whether a factor should be retained. Finally, three factors were identified for each study phase.

We labeled dietary patterns based on the data interpretation and literature. Also we considered the food groups in each factor in three phases. For each participant, a factor score for each identified pattern in each phase was computed by summing up the intakes of food groups weighted by their factor loadings, obtained based on the PCA analysis. A high factor score for a particular pattern means greater adherence to that dietary pattern and vice versa. We assessed the dose–response effects of dietary patterns score because of longitudinal structure of study and repeated measurements of dietary patterns score.

Quantitative and qualitative variables were expressed as mean ± s.d. and counts (percent), respectively. Student-t or Mann–Whitney U (if the normality assumption was not held) tests were performed to evaluate significant differences in quantitative variables across MetS status. The association of categorical variables and MetS status was assessed by applying chi-square tests.

The Kolmogorov–Smirnov test indicated that the entire dietary patterns were positively skewed; therefore, log-transformed dietary patterns were considered in the modeling procedure as covariates.

The nonparametric test was performed for trend analysis across time. It was developed by Cuzick (1985) [27], which is an extension of the Wilcoxon rank-sum test. In this study, the trend of the mean of the quantitative variables and proportion of qualitative variable across time (i.e. the three phases of study) was tested. This test was done separately for MetS and non-MetS participants.

We performed a multivariate analysis to evaluate the longitudinal associations of dietary patterns scores with MetS and a number of MetS components as repeated measurements using mixed effects logistic and cumulative logit regressions, respectively and with time-variant covariates taken into account. These models accommodated overdispersion and longitudinal structure through two separate sets of random effects, conjugate random effects at the level of the mean for the first aspect and normal random effects embedded within the linear predictor for the second aspect [28]. The models were adjusted for age, sex, socioeconomic status, smoking status, physical activity, BMI and medications for hypertension and diabetes. We treated confounders (SES, smoking status, physical activity, BMI and medications for hypertension and diabetes) as time-varying covariates with three measurements.

Energy intake adjustment is important in nutritional epidemiological studies to control the confounding effects of energy intake and body size. However, owing to the lack of data on energy intake in the current study, such adjustment was achieved using BMI and, additionally, physical activity as suggested by Jakes and et al. [24].

Models including categorical forms of dietary patterns were further examined to assess whether modeling the association between MetS and number of MetS components and each of the continuous dietary patterns as linear was appropriate. Considering dietary patterns as categorical variables, deteriorated the result. Therefore, the best model was chosen based on the model selection criteria.

SAS software, version 9.3 (SAS Institute Inc.) was used to perform all statistical analyses. P-values <0.05 (two-tailed) were considered as statistically significant.

Results

General characteristics of participant in three phases of the study across MetS status are presented in Table 2. The prevalence of MetS was 34.4%, 33.3% and 45.3% of the study population in three phases (P for trend < 0.001), respectively. The participants with MetS were older, had higher BMIs and lower socioeconomic status (P < 0.01) and were less likely to be physically active (P < 0.001) than the subjects without MetS. All MetS components were significantly different between the absence and presence of MetS (P < 0.001).

Three major dietary patterns were identified that explained 29.56%, 27.58% and 26.20% of the total variance in three phases of the study, respectively. The Healthy diet was characterized by high intake of fruits and vegetables as well as olive oil, chicken and fish. Nuts and beans also fell in this pattern in phase 2 and 3 indicating greater adherence to a Healthy diet in recent year in the Iranian population. The Iranian diet contained high intakes of Iranian traditional product, such as dairy products, animal fat, sweets and organ meat. Red meat and hydrogenated oil fell in this pattern in phase 2 and 3. The Western diet was greatly loaded with frequent consumption of fried foods, rice, red meat, hydrogenated oil, carbonated beverages, fast food and canned food. Also, sweets fell in the Western pattern in phase 2 and 3 (Table 3). As seen in Table 2, all dietary patterns had a significant trend in the score during thirteen years follow-up in both groups (P for trend < 0.001).

The result of mixed effects Logistic and cumulative logit regressions adjusting for potential confounders were

Table 2 General characteristics of study population and comparison for subjects with and without metabolic syndrome in three phases of Isfahan cohort study.

	2001			2007			2013			P for trend*	
	MetS (+) N = 477	MetS (−) N = 910	P-value	MetS (+) N = 462	MetS (−) N = 925	P-value	MetS (+) N = 628	MetS (−) N = 759	P-value	MetS (+)	MetS (−)
Age (years) [mean ± SD]	49.13 ± 9.07	46.55 ± 9.14	<0.001	48.95 ± 9.16	46.68 ± 9.13	<0.001	47.86 ± 8.74	47.08 ± 9.55	0.008	0.016	0.39
Female (%)	72.5	40.3	<0.001	64.1	45.1	<0.001	62.1	42.6	<0.001	<0.001	0.31
SES (%)			<0.001			0.03			<0.001	0.23	0.83
Low	39.6	26.9		39.4	31.2		38.4	29.2	–	–	–
Moderate	37.7	37.4		31	31.2		33.8	32	–	–	–
High	22.6	35.7		29.7	37.5		27.9	38.7	–	–	–
Smoker (%)	10.3	26.9	<0.001	16.7	22.6	0.01	17.7	20.8	0.141	0.001	0.003
Physical activity (METS) [mean ± SD]	13.3 ± 9.25	16.42 ± 9.39	<0.001	13.73 ± 7.86	15.07 ± 9.9	0.02	11.66 ± 8.53	13.68 ± 10.71	<0.001	0.001	<0.001
BMI (kg/m^2) [mean ± SD]	30.11 ± 4.41	26.22 ± 4.33	<0.001	29.82 ± 4.01	26.73 ± 4.23	<0.001	29.82 ± 4.37	26.6 ± 4.3	<0.001	0.35	0.07
WC (cm) [mean ± SD]	104.88 ± 9.18	94.22 ± 10.59	<0.001	100.07 ± 9.17	91.07 ± 10.98	<0.001	102.92 ± 9.6	93.34 ± 10.75	<0.001	0.002	0.095
SBP (mm Hg) [mean ± SD]	128.69 ± 20.68	114.65 ± 15.88	<0.001	132.76 ± 17.81	120.26 ± 17.36	<0.001	134.4 ± 16.71	123.9 ± 17.02	<0.001	<0.001	<0.001
DBP (mm Hg) [mean ± SD]	82.42 ± 12.43	73.87 ± 10.36	<0.001	82.01 ± 10.3	76.45 ± 9.94	<0.001	85.25 ± 13.29	80.9 ± 11.32	<0.001	<0.001	<0.001
TG (mg/dL) [mean ± SD]	250.07 ± 109.77	175.85 ± 103.78	<0.001	243.13 ± 131.33	136.63 ± 86.51	<0.001	194.53 ± 97.33	122.74 ± 54.89	<0.001	<0.001	<0.001
FPG (mg/dL) [mean ± SD]	95.97 ± 39.41	82.06 ± 21.3	<0.001	119.84 ± 51.45	92.74 ± 26.59	<0.001	120.79 ± 48.18	94.99 ± 20.63	<0.001	<0.001	<0.001
HDL (mg/dL) [mean ± SD]	43.65 + 9.69	48.78 ± 10.3	<0.001	41.81 ± 9.95	49.08 ± 11.24	<0.001	40.83 ± 17.75	47.65 ± 24	<0.001	<0.001	<0.001
Healthy diet [mean ± SD]	10.15 ± 5.24	9.67 ± 5.25	0.14	21.35 ± 7.06	21.4 ± 7.32	0.91	7.42 ± 3.92	7.32 ± 4	0.40	<0.001	<0.001
Iranian diet [mean ± SD]	3.83 ± 3.88	4.46 ± 3.87	<0.001	11.12 ± 5.32	11.09 ± 4.77	0.64	23.23 ± 10.04	22.8 ± 9.66	0.77	<0.001	<0.001
Western diet [mean ± SD]	10.92 ± 4.47	11.20 ± 4.37	0.26	4.69 ± 3.11	5.24 ± 2.94	<0.001	4.75 ± 3.2	5.31 ± 3.14	<0.001	<0.001	<0.001

Quantitative variables were expressed as mean ± s.d. and qualitative variables were expressed as percent.

SES, socioeconomic status; WC, waist circumference; SBP, Systolic blood pressure; DBP, Diastolic blood pressure; TG, Triglyceride; FPG, Fasting plasma glucose; HDL, High-density lipoprotein cholesterol.

*P for trend in three phases of study for with and without Metabolic Syndrome.

Table 3 Factor-loading matrix for the major factors (diet patterns) identified by using food consumption data from the food-frequency questionnaire used in the Isfahan Cohort Study in three phases.

Food groups	Phase 1			Phase 2			Phase 3		
	Dietary patterns			Dietary patterns			Dietary patterns		
	Healthy	Iranian	Western	Healthy	Iranian	Western	Healthy	Iranian	Western
Liquid oil	0.665			0.418				0.403	
Fish	0.576			0.422			–	–	–
Chicken	0.563			0.349			–	–	–
Fruits and vegetables	0.536			0.560			0.343	0.657	
Olive oil	0.428			0.549			0.591		
Whole dairy product		0.691		0.424				0.640	
Animal fat		0.651			0.476			0.352	
Sweets		0.571				0.455			0.394
Organ meats		0.504		–	–	–			0.210
Pickles		0.364			0.485				0.353
Nuts		0.329		0.509			0.605		
Fried food			0.625			0.498			0.672
Rice			0.560			0.520			0.435
Red meat			0.506		0.575			0.352	
Hydrogenated oil			0.502		0.335				0.234
Carbonated beverages			0.436			0.524			0.525
Fast foods			0.334			0.593			0.522
Beans			0.312	–	0.491	–	0.387		
Canned food			0.303			0.301			0.323
Bread	–	–	–		0.498			0.573	

Foods or food groups with factor loadings < 0.2 for all factors were excluded.

reported in Table 4. After controlling for age, sex and SES, the higher scores (high intake) of the Healthy diet during the 13 year follow-up was significantly associated with a lower risk of MetS and fewer number of MetS components (OR: 0.50, 95% CI: 0.36–0.69, OR: 0.49, 95% CI: 0.37–0.66, respectively). In contrast, the higher scores (high intake) of the Iranian diet during the 13 year follow-up was associated with greater risk of MetS and higher number of MetS components (OR: 1.74, 95% CI: 1.35–2.25, OR: 2.05, 95% CI: 1.63–2.58, respectively). Further adjustment for other potential confounders weakened these associations slightly, but they remained significant. Even after additional control for BMI and medications for hypertension and diabetes, the inverse association of the healthy dietary pattern score and the positive association of the Iranian dietary pattern score with the MetS and number of MetS components remained significant. One unit increase in Healthy diet score in a subject, while keeping other variables in the model fixed, was associated with 50% and 48% reduction in the risk of MetS and the number of MetS components, respectively. Also, one unit increase in long-term intake of an Iranian diet in a subject, while keeping other variables in the model fixed, was associated with 1.28 and 1.45 times higher odds of having MetS and higher number of MetS components, respectively. The Western diet did not show significant association even after additional control for BMI and medications for hypertension and diabetes (OR: 1.14, 95% CI: 0.76–1.71, OR: 1.19, 95% CI: 0.83–1.70, respectively). However, after adjustment for medications for hypertension and diabetes, the surprising negative association of the Western dietary pattern disappeared, and the result showed a positive association.

Table 4 Odds Ratios and 95% Confidence Intervals for Metabolic Syndrome and number of Metabolic Syndrome Components According to Dietary Pattern Score.

	Crude model	Model 1	Model 2	Model 3	Model 4
MetS (yes/no)					
Healthy dietary pattern[a]	0.46 (0.33–0.64)	0.50 (0.36–0.69)	0.54 (0.39–0.74)	0.48 (0.35–0.67)	0.50 (0.36–0.70)
Iranian dietary pattern[a]	1.44 (1.12–1.86)	1.74 (1.35–2.25)	1.70 (1.32–2.20)	1.58 (1.23–2.04)	1.28 (1.01–1.65)
Western dietary pattern[a]	0.52 (0.35–0.78)	0.76 (0.51–1.15)	0.79 (0.52–1.2)	0.82 (0.54–1.23)	1.14 (0.76–1.71)
Number of MetS components					
Healthy dietary pattern[a]	0.46 (0.36–0.61)	0.49 (0.37–0.66)	0.53 (0.4–0.71)	0.49 (0.37–0.66)	0.52 (0.39–0.70)
Iranian dietary pattern[a]	1.75 (1.4–2.21)	2.05 (1.63–2.58)	2.02 (1.61–2.54)	1.89 (1.51–2.37)	1.45 (1.16–1.81)
Western dietary pattern[a]	0.53 (0.37–0.77)	0.75 (0.52–1.08)	0.78 (0.54–1.12)	0.78 (0.54–1.12)	1.19 (0.83–1.70)

Data are expressed by odds ratio (95% CI).
Model 1: adjusted by age, sex, socioeconomic status.
Model 2: adjusted by age, sex, socioeconomic status, smoking status and physical activity.
Model 3: adjusted by age, sex, socioeconomic status, smoking status, physical activity and BMI.
Model 4: adjusted by age, sex, socioeconomic status, smoking status, physical activity, BMI and medications for hypertension and diabetes.
[a] On logarithmic scale due to non-normality.

Discussion

This longitudinal study examined the long-term dose−response relationship between dietary patterns and risk of MetS and number of MetS components among Iranian population during 13 years of follow-up. Three major dietary patterns were identified in three phases: Healthy, Iranian and Western dietary patterns. The Iranian dietary pattern was positively associated with risk of MetS and number of MetS components. The Healthy dietary pattern was inversely associated with risk of MetS and number of MetS components. These associations persisted in multivariate models accounting for potential confounders including BMI and medications for hypertension and diabetes. We did not find any statistically significant association between Western diet and MetS. To the best of our knowledge, this study is the first longitudinal cohort study from Iran with repeated measurements of dietary intake that reports the longitudinal association between major dietary patterns and risk of MetS and number of MetS components.

The Iranian dietary pattern we identified was positively associated with the risk of MetS and number of MetS components. This finding might be attributed to the mechanism of carbohydrate and fat in the Iranian diet which is completely different from beneficial diets on metabolic risk factors consumed in Asian countries, which are rich in whole grains rather than refined grains [29,30]. The studies have demonstrated that it is not the quantity but the quality of carbohydrates which increases the risk of MetS [8,11]. It is now well established that high-carbohydrate diets, particularly from refined sources, lower HDL cholesterol and raise triglycerides, the most prevalent components of dyslipidemia among Iranians [30,31]. Also, it is not the amount but the quality of fat: omega-3 from fish in Japan, olive oil (rich in MUFA and polyphenolics) in Mediterranean countries and mustard oil in India (omega 3 and MUFA), which have been found protective. Nevertheless, our Iranian pattern was characterised by elevated intake of refined carbohydrate and fat, notably saturated fat likely to contribute to the pathogenesis of various components of the metabolic syndrome, and to the increased risk of cardiovascular diseases (CVD) and type 2 diabetes over time. The previous study demonstrated that the mean trans-fatty acid content of hydrogenated oils produced in Iran (34.6 $\pm$ 6.6%, range: 22.5−46.2%) is much higher than the recommendation of the World Health Organization [32].

In the present study, the Healthy dietary pattern showed a protective effect on MetS and was inversely associated with the number of MetS components, confirming the results of previous studies. The Healthy diet we identified in the current study is somewhat similar to the Mediterranean diet reported in other studies, which has received significant attention regarding its apparent protective effect against MetS [6,7,33]. Several epidemiological cross-sectional studies, RCTs, and prospective studies have reported an inverse association between MetS and the Mediterranean diet [6−9,13,34,35]. The beneficial effect of the Mediterranean diet might be explained by higher amounts of antioxidants including flavonoids, carotenoids, and vitamins C and E, as well as monounsaturated and polyunsaturated fatty acids [30,36−38]. However, it has been hypothesized that the key to its benefits does not rely on single components, but rather on a synergic effect of each food characteristic of this dietary pattern [5,39].

We found no significant association between the long-term intake of the Western dietary pattern and MetS and the number of MetS components. The results are in agreement with several previous studies [6,7]. It is plausible that red meat and hydrogenated oil, two items of the Western dietary pattern in other studies, are major food items in the Iranian diet, therefore reduce the high quantities of refined carbohydrate and fat in the Western pattern. Unfortunately, we could not control for total energy intake in the current study, which might also provide a reason; however, controlling for BMI, as a surrogate for energy intake, did not alter the findings.

The current study provides useful information to clarify the longitudinal effect of dietary habits on MetS and number of MetS components in a longitudinal analysis in the Iranian population who has, until now, not been studied adequately. Most previous studies relating MetS to diet were cross-sectional. Thus, the prospective design of our study, in which dietary behaviors and outcome variables were assessed with repeated measurements during long follow-up (13 years), strengthen the findings. However, several limitations need to be considered in interpreting our results. First, the FFQ used in the present study was a short FFQ, which could roughly assess usual dietary habits in the Iranian population. Second, although most of the epidemiological evidence on the association between diet and disease come from quantitative FFQs [7−9,11−15,34]; the FFQ used in this study did not have data on portion sizes; therefore, we could not measure total energy intake in this study. Using BMI as a surrogate for energy intake might not be clinically valid because some individuals, including those engaged in manual work, will have high energy intakes and low BMI. Therefore, we further adjusted our model for physical activity during statistical analysis [24]. Finally, the observational cohort design of our study with repeated measurements implies that dietary measurements were conducted at the same time as the outcome measurements, thus reverse causation bias may have occurred. RCT is thus needed to identify causality.

In conclusion, we found that greater adherence to the Healthy diet was associated with lower risk of MetS. In contrast, long-term consumption of the Iranian diet which is high in saturated fat and refined carbohydrate was positively associated with the risk of MetS in the Iranian population.

Contributors

RH and MM participated in the statistical analyses, data interpretation and manuscript drafting. IK participated in the statistical analyses and data interpretation. MS, NM, HR, NZ and MT participated in the study design and data

interpretation. All authors have revised the manuscript for important intellectual content and read and approved the final version of the manuscript.

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