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Original article

Long-term nuts intake and metabolic syndrome: A 13-year longitudinal population-based study

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SUMMARY

Background & aims: The ability of nuts to improve the conditions of the metabolic syndrome (MetS) is now well established. However, few longitudinal studies examined the impact of nuts on MetS and those that have been ongoing considered baseline measurement of nuts intake. The associations between nuts intake and the risk of MetS was longitudinally assessed in our study using repeated measurements of nuts intake.

Methods: The population-based longitudinal study was conducted on a sub-sample of the Isfahan Cohort Study (ICS), including 1387 adults, aged ≥ 35 years. A validated food frequency questionnaire was applied to obtain data on the nuts intake. International Diabetes Federation (IDF) criteria were used to define MetS. The longitudinal relation between the trend of nuts intake and the risk and severity of MetS was examined using the Logistic and Cumulative Logit regressions with considering mixed random effects.

Results: After adjustment for potential confounders, a statistically significant inverse association was found in severity of MetS (the number of positive criteria) in the second quartile of nuts compared with the lowest quartile (OR: 0.77, 95% PI: 0.63–0.96; P trend: 0.03). Nuts intake was inversely associated with MetS risk among participants in the second quartile compared with the lowest quartile (OR: 0.76, 95% PI: 0.59–0.96; P trend: 0.14).

Conclusions: Nuts intake demonstrated a significant, inverse association with the risk and severity of MetS after a 13-year follow-up period in a cohort of the Iranian population.

1. Introduction

The prevalence of the metabolic syndrome (MetS), related outcomes and presence of concomitant diseases such as type-2 diabetes and cardiovascular disease (CVD) is continuously increasing [1]. Currently, MetS roughly affects 20–30% of adults worldwide, and evidence shows an upward trend in the rate [2]; in Iran, the prevalence is 33.8% [3,4]. A group of the most important CVD risk factors, including glucose metabolism disturbances, abdominal adiposity, dyslipidemia, and hypertension define the MetS [5]. Having increased prevalence of the metabolic syndrome and type-2 diabetes [2], it is essential to identify diet and lifestyle modifications among other contributing factors for primary prevention policy [6].

Based on the current scientific evidence, nuts may be a useful constituent of a dietary regimen because of their exclusive nutritional values [7]. Nuts are rich in healthy fatty acid profile, as well as being good sources of dietary fiber, minerals, vitamins, and other bioactive ingredients, including tocopherols, phytosterols, and polyphenols [8–12]. Therefore, nuts can protectively influence the

Abbreviations: ICS, Isfahan Cohort Study; ICRC, Isfahan Cardiovascular Research Center; SES, socioeconomic status; PI, probability interval; PA, physical activity; FA, factor analysis.

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individual characteristic of MetS and thus the whole MetS and consequently diabetes and CVD [13].

Although, the assessment of nuts intake and MetS is increasingly under consideration, there is still inadequate surveys examining the association between nuts intake and MetS, and they reported inconsistency results relying on variations in the assessment or definition of nuts intake [14–18].

Some cross-sectional studies reported that nuts intake results in reducing the risk of MetS or its components [15–18]. The beneficial effect of nuts intake on oxidative stress [19], endothelial function [20], inflammation [21], hypertension, insulin resistance, diabetes, obesity, and subsequently the reducing risk of CVD have been shown in different clinical trials [22,23]. However, it is of great importance to identify the impact of long-term nuts consumption on the risk of MetS.

In a 6-year prospective study, nuts intake (tree nuts + peanuts) was related to lower incidence of MetS [14]. Other prospective study investigated total and various types of nut (separately) with the incidence of MetS. They observed nuts intake of five or more serving per week statistically decrease the incidence of MetS. Walnut intake showed a significant, negative relation with MetS risk [6]. A few longitudinal studies have examined the relation between nuts intake and MetS; they were mostly limited to explore the association between the baseline measurement of the Mediterranean or prudent diet included or supplemented with nuts and MetS [24–27]. Thus, it is necessary to perform longitudinal studies with repeated-measurement intake of nuts as to analyze whether long-term intake of nuts is associated with the MetS. Also, in the literature, the Mets severity, defined as the number of positive criteria [26,28], was not considered and all of them concentrated only on the incidence of MetS. Thus, the repeated-measurement information on MetS is lacking. To our knowledge, there is a longitudinal study assessed the repeated measurement of dietary patterns and Mets severity that reported the healthy dietary pattern included nuts decrease the severity of MetS [28]. Also, Iranian diet demonstrated as an important factor for increasing the risk of MetS and the number of its components. Iranians intake refined grains more than whole grains, unlike other Asian countries. Moreover, refined carbohydrate and saturated fat widely consumed in Irian diet, contribute to MetS components. However, Iranian people consume nuts a lot as a meal and snack, and also in their traditional Iranian festivals such as *Nowruz* (the name of the Iranian New Year) and *Shab-e Yalda* (celebrated on the longest night of the year). Thus, it is important to evaluate its impact on MetS. The novelty of our study is not only taking into account nuts intake but also the outcome variable in repeated measurement settings. Thus, in addition to covariates being considered time-varying, the outcome changes were monitored during 13-year follow-ups.

We thus examined the long-term association between nuts intake and the risk of developing MetS regarding the severity of MetS, in a central Iranian population cohort. Moreover, the association between the presence of MetS was longitudinally examined.

2. Materials and methods

2.1. Study population

A sub-sample of 6504 adults aged equal or more than 35 years old from Isfahan Cohort study (ICS), as a prospective community-based survey, was used in our research. The ICS was previously described in details [29]. The subjects are from three central areas of Iran. They were recruited from January to September 2001, using multistage random sampling based on their sex, age and residence type (urban/rural) distribution. The participants were followed biannually to detect major cardiovascular events. The main aim of the ICS is to evaluate the relation of different life-style behavior, anthropometric measurements, and biochemical markers with the risk of CVD events. The Ethics Committee of Isfahan Cardiovascular Research Center (ICRC), as a World Health Organization-collaborating center, approved our study. Having obtained an informed written consent, the participants underwent laboratory measurements, physical examination, and interview. Measurements in the baseline phase of the study were repeated for whom without any CVD events in 2007 and for a subsample in 2013. A number of 1387 baseline participant, those who had complete information and also attended in both 2007 and 2013 repeated measurements were enrolled in our study. More investigation presented that there was no significant difference (P-value = 0.1) in intaking of nuts between those participants lost to follow-up compared with those remained in the study. The mean of nuts intake was 1.2 ± 2.2 and 1.1 ± 2.3 in followed-up and non-followed-up groups, respectively. The protocol that was used in 2007 and 2013 survey was similar to what was used in 2001.

2.2. Metabolic syndrome definition

International Diabetes Federation (IDF) criteria were used to define MetS [30], if the study participants had central obesity defined as waist circumference ≥ 90 cm (men) or ≥80 cm (women) in Asian population, plus any two of the following criteria: (1) high triglycerides defined as fasting triglycerides ≥ 150 mg/dL or lipid medications; (2) low HDL cholesterol defined as HDL cholesterol < 40 mg/dL (men) or <50 mg/dL (women) or lipid medications; (3) high fasting plasma glucose defined as fasting plasma glucose ≥ 100 mg/dL or use of diabetes medications; and (4) high blood pressure defined as SBP ≥ 130 mmHg, DBP ≥ 85 mmHg, or use of antihypertensive medications.

In our study, the severity of MetS was assessed as the number of positive criteria [26,28] (ordinal scale).

2.3. Dietary assessment

A simplified 48-item food frequency questionnaire (SFFQ) was used to acquire dietary intake information over the three times of study through a face-to-face interview [31]. The validity and reproducibility of SFFQ were examined elsewhere [31]. The daily, weekly and monthly (a.k.a., frequency) intake of each food item in a previous year was reported by the participants. Weekly intake was used for the entire frequencies, and 'zero' was used in cases of 'never' or 'rare' food consumption. Nuts intake was calculated by summing up the weekly intake of pistachio, almond, hazelnut, walnuts, and seeds.

Spearman's rank correlation coefficients between nuts intake accessed by simplified food frequency questionnaire and quantitative amount of food intake assessed by mean of single 24 h recall and two food records were 0.468 (P < 0.001) in total population and 0.465 (P < 0.001) and 0.479 (P < 0.001) in male and female, respectively. ICC for reproducibility of FFQ for nuts intake was o.67 (0.40–0.93), 0.64 (0.40–0.89) and 0.65 (0.39–0.92) in total population, male and female, respectively. The cross-classification frequency intake of nuts between the SFFQ and the reference method revealed that 50% of participants were classified in the same quartile of two methods.

To obtain total dietary score, foods items are first categorized in 12 groups defined as: (1) white meat, (2) dairy products, (3) vegetables, (4) fruits, (5) nuts, (6) legumes, (7) non-hydrogenated vegetable oils, (8) processed meat, (9) red meat, (10) hydrogenated vegetable oils, (11) grains, (12) sweets and pizza. Second, individuals were divided into quintiles according to their intakes of foods from these groups. A score of one has been assigned to the

participants with the fourth and fifth intake quintiles for the healthy diet (groups (1)–(7)), whereas a score of zero has been given to the three smallest intake quintiles. In contrast, reverse scoring was applied to the unhealthy diet. Finally, the sum of food groups scores was calculated to obtain the total dietary score which varies between 0 and 12 [32].

2.4. Assessment of other covariates

Participants completed standardized questionnaires on socio-economic and demographic properties, and life-style components (nutrition, smoking, and physical activity). Whole information about individuals was gathered by trained health professionals.

Medical interviews and physical examinations were conducted by trained physicians. Standard protocols were applied to measure blood pressure and anthropometric measurements. The lipid profiles and glucose levels were measured using fasting blood samples.

The factor analysis (FA) was used to quantify socioeconomic status (SES). We used FA with only one extracted factor to obtain factor score. Such a score was used to group the subjects into tertiles. In the FA, the education level, income, and occupation type were used. The population economically dependent on the active age group was considered by adding the number of those aged <18 or >65 and those aged 18–65 at home. Those who were in the lowest, second and highest score tertiles were labeled as low, medium, and high SES, respectively.

Smokers were defined as those who smoke one or more cigarettes per day while ex-smokers were defined as those who were smoking previously and are non-smoker currently. They, in addition to non-smokers, constitutes the smoking status variable in our study.

The Iranian version of International Physical Activity Questionnaire (IPAQ), was used to assess physical activity (i.e., metabolic equivalent hours per week (MET-h/wk.)). The reliability and validity of IPAQ were verified in several studies [33–35]. It included questions on household, leisure time, transportation and occupational items. The total physical activity was obtained by summing up questions in all items.

2.5. Statistical analysis

Continuous and categorical variables were presented as mean ± s.d. and counts (percent), respectively. The nonparametric test introduced by Cuzick (1985) [36] was used to assess changing the means and the proportions in three study phases. Trend analysis was also done across the quartiles of nuts intake. To examine the overall trend of the odds ratios (ORs) of MetS across quartiles of nuts intake, the nuts was used as a continuous variable in the models.

The longitudinal relation of nuts intake with MetS and the severity of MetS (the number of positive criteria) -as repeated measurements- was evaluated using a multivariate analysis. The mixed-effect regression via logit or cumulative logit link functions with time-variant covariates were used in our study. Two separate non-normal and normal random effects were used for managing both over-dispersion and longitudinal nature of data, respectively [37]. Because of the model complexity, the Bayesian approach was used to estimate parameters. The odds ratios and 95% Bayesian probability intervals (PI) for MetS and the severity of MetS across quartiles of nuts were estimated based on four modeling processes: 1) crude model; 2) adjusted model by age, sex, SES, smoking status, total physical activity, medications for hypertension, diabetes, and hyperlipidemia; 3) additionally adjusted by total dietary score; 4) further adjusted for BMI. We treated confounders as time-varying covariates.

We considered the deviance information criterion (DIC) [38] and the Bayesian P-value (BP) [39], the most common criteria for Bayesian model choice. Fitted models with lower values of DIC and a BP near 0.5 are preferred.

In this study, concerning insufficient data on energy intake, energy-adjusted intake of nuts for each study year, was calculated based on BMI as a surrogate measure [28,40,41] using the residual method [42]. Individuals were categorized based on the quartiles of nuts-BMI adjusted intake.

Statistical analyses were performed, using SAS software, version 9.3 (SAS Institute Inc.) and OpenBUGs software, version 3.2.3. P-values < 0.05 (two-tailed) were considered as statistically significant.

3. Results

Table 1 illustrates the general characteristics of participants across quartiles of nuts intake in three study times. Participants in the higher quartiles of nuts intake had a higher SES ($P < 0.001$), were more likely to be physically active ($P < 0.001$) and had a higher dietary score ($P < 0.001$) in all three times of study. At first examination in 2001, participants who consumed more nuts had lower BMI ($P < 0.001$), WC ($P < 0.001$), TG ($P = 0.001$) and the number of MetS positive criteria ($P < 0.001$) and were less likely to have MetS ($P = 0.003$) and hypertension ($P = 0.011$). No statistically significant trends were observed in second and third examination across quartiles of nut intake.

With regard to the trend analysis across follow-up time, the characteristics of the subjects had changed from 2001 to 2013 (Table 2). The prevalence of hypertension and hypertriglyceridemia had decreased significantly during the study period for both sex and total population ($P < 0.001$). Moreover, high FPG, and low HDL-C had increased ($P < 0.001$). Central obesity had increasing trend in male ($P = 0.001$) and slightly decreasing trend in female ($P = 0.015$). MetS prevalence in male ($P = 0.045$) and number of MetS positive criteria in male and total population ($P < 0.001$) showed significant increasing trend across time. A considerable rise existed in nuts intake in the second examination in 2007; however, it decreased again in the third examination in 2013.

The adjusted ORs (95% PI) resulted from two regressions were presented in Table 3. A statistically significant reduction has been found in MetS risk, among the second versus the lowest quartile of nuts intake in the crude model (OR: 0.74, 95% PI: 0.57–0.94). The MetS severity was defined as the number of positive criteria, decreased among the second versus lowest quartile of nuts intake (OR: 0.75, 95% PI: 0.60–0.94). In the adjusted model, subjects in the second quartile had a 24% and 22% lower risk of MetS and number of positive criteria (OR: 0.76, 95% PI: 0.59–0.97; OR: 0.78, 95% PI: 0.63–0.97) compared with those in the first quartile. After adjustment for dietary intakes, these associations were persisted. Participants in the second quartile had a 24% lower risk of MetS (OR: 0.76, 95% PI: 0.59–0.96) compared with those in the first quartile. Also, a statistically significant decrease has been found in severity of MetS among the second versus the lowest quartile of nuts intake (OR: 0.77, 95% PI: 0.63–0.96; P for trend: 0.03). These significant associations disappeared after further adjustment for BMI.

Model comparisons showed that the full adjusted model had the best fit based on DIC criteria for both MetS occurrence and severity models. According to Bayesian P-value criteria, all models showed desirable fit for MetS severity. However, for both MetS occurrence and severity, the crude model is the best based on Bayesian P-value criteria.

Table 1
General characteristics of study population across quartiles of nuts intake in each study year.

	2001				P trend[c]	2007				P trend[c]	2013				P trend[c]
	Nut quartiles					Nut quartiles					Nut quartiles				
	1st (n = 346)	2nd (n = 347)	3rd (n = 347)	4th (n = 347)		1st (n = 346)	2nd (n = 347)	3rd (n = 347)	4th (n = 347)		1st (n = 346)	2nd (n = 347)	3rd (n = 347)	4th (n = 347)	
Age (years)[a]	49.5 ± 9.6	49.7 ± 10.4	45.7 ± 7.7	44.9 ± 7.8	<0.001	48.7 ± 9.7	46.6 ± 8.9	46.9 ± 9.1	47.5 ± 9	0.142	47.4 ± 9.3	47.1 ± 9.5	47.3 ± 9	47.9 ± 9	0.263
Female[a]	65	41.8	48.4	50.4	0.002	53.5	47.6	49.3	55.3	0.541	58.4	44.4	50.1	52.7	0.354
SES					<0.001					<0.001					<0.001
Low	39	37.2	22.2	26.8		47.4	31.7	29.4	27.4		44.5	33.1	30.5	25.4	
Moderate	35.3	33.4	40.6	40.6		30.9	34	29.4	30.3		31.2	37.5	31.4	31.1	
High	25.7	29.4	37.2	32.6		21.7	34.3	41.2	42.4		24.3	29.4	38	43.5	
Smoker	10.1	19.6	13.3	19	0.011	13.3	15.9	11.6	9.8	0.160	12.7	14.4	13.5	12.7	0.571
PA (METS)	13.1 ± 8.2	15.2 ± 9.3	16.1 ± 9.5	16.9 ± 10.3	<0.001	13.3 ± 8	13.8 ± 7.7	15.5 ± 10.5	15.9 ± 10.4	<0.001	11.6 ± 9.3	13 ± 11.1	13.2 ± 9.1	13.3 ± 9.7	<0.001
BMI (kg/m^2)	30.5 ± 3.6	24.8 ± 4	27.7 ± 4.8	27.2 ± 4.7	<0.001	28 ± 4.5	27.6 ± 4.5	27.5 ± 4.2	27.9 ± 4.3	0.828	28.6 ± 4.8	27.4 ± 4.5	28.3 ± 4.7	27.9 ± 4.4	0.419
High WC	97.4	70.9	81.8	81.6	<0.001	78.3	75.8	75.5	80.1	0.612	85.5	82.1	86.7	86.2	0.449
HTN	38.4	28.2	36.3	26.2	0.011	45.4	40.1	40.3	40.6	0.240	27.1	21.7	22.3	26.8	0.979
Hyper.TG	74	53	64.3	57.3	0.001	47.4	49.3	44.7	47.6	0.729	43.9	37.8	45	42.9	0.712
High FPG	18.5	11.2	12.1	13.3	0.073	28.3	26.2	26.2	29.4	0.764	41	37.8	38.3	46.4	0.158
Low HDL-C	46.5	44.4	44.1	45.2	0.729	47.4	42.1	43.5	45.5	0.729	63.2	52.2	63.4	59.4	0.989
Dietary intake	4.8 ± 1.9	4.6 ± 1.8	5.4 ± 1.7	5.5 ± 1.7	<0.001	4.3 ± 1.7	4.3 ± 1.7	5.3 ± 1.9	6.4 ± 1.9	<0.001	4.4 ± 1.7	4.5 ± 1.8	5.6 ± 1.9	6.6 ± 1.9	<0.001
MetS (+)	57.2	35.4	48.4	41.2	0.003	46.2	42.1	40.9	45.5	0.784	47.1	42.9	49.3	47.3	0.570
Severity of MetS[b]					<0.001					0.6					0.435
≤2 components	41.9	63.7	50.7	58.5		51.7	55.6	56.8	52.4		51.7	55.3	49.3	50.1	
3 components	35.5	26.5	32.9	29.4		26	23.1	23.9	26.8		20.5	25.1	27.7	21	
4 components	18.2	8.6	14.7	11.2		16.5	14.7	15.6	16.1		14.2	12.7	13	17.3	
5 components	4.3	1.2	1.7	0.9		5.8	6.6	3.7	4.6		13.6	6.9	10.1	11.5	

Quantitative variables were expressed as mean ± s.d. and qualitative variables were expressed as percent.
SES, socioeconomic status; PA, physical activity; BMI, body max index; WC, waist circumference; HTN, hypertension; Hyper.TG, Hypertriglyceridemia; FPG, Fasting plasma glucose; HDL-C, High-density lipoprotein cholesterol. High WC: waist circumference ≥90 cm (men) or ≥80 cm (women) in Asian population; HTN: SBP > 130 mmHg, DBP > 85 mmHg or use of antihypertensive medications; Hyper.TG: fasting triglycerides > 150 mg/dL or lipid medications; High FPG: fasting plasma glucose ≥ 100 mg/dL or use of diabetes medications; Low HDL-C: HDL cholesterol < 40 mg/dL (men) or <50 mg/dL (women).

[a] Age and sex are time-constant variables and others considered as time-vary variables.

[b] Calculated as the number of positive criteria.

[c] P for trend across nuts quartiles in each study year.

Table 2
Trend in MetS components and nut intake during 13-year follow-up.

	Male			P for trend	Female			P for trend	Total			P for trend[c]
	2001	2007	2013		2001	2007	2013		2001	2007	2013	
High WC[a]	69.7	63.5	77.9	0.001	95.4	90.6	92	0.015	82.9	77.4	85.1	0.127
HTN[a]	32.2	46.4	21.8	<0.001	32.4	37	27	0.029	32.3	41.6	24.5	<0.001
Hyper.TG[a]	66.6	50	41.5	<0.001	57.9	44.6	43.3	<0.001	62.1	47.2	42.4	<0.001
High FPG[a]	12.5	27.3	40.5	<0.001	15	27.8	41.2	<0.001	13.8	27.5	40.9	<0.001
Low HDL-C[a]	30.4	38.6	54.1	<0.001	58.9	50.4	64.7	0.029	45.1	44.6	59.5	<0.001
MetS (+)	37.8	38.9	43.2	0.045	52.9	48.2	49.9	0.269	45.6	43.7	46.6	0.569
Severity of MetS[b]				<0.001				0.140				<0.001
≤ 2 components	61.1	57.1	54.2		46.7	51.3	49.2		53.7	54.1	51.6	
3 components	28.9	22.8	25.5		33.1	26.9	21.7		31.1	24.9	23.6	
4 components	8.9	15.6	11.9		17.3	15.8	16.5		13.2	15.7	14.3	
5 components	1	4.5	8.5		2.9	5.9	12.5		2	5.2	10.5	
Nut intake	1.2 ± 1	4 ± 1	2.6 ± 0.9	<0.001	1.2 ± 1	4 ± 1	2.7 ± 1.1	<0.001	1.2 ± 1	4 ± 1	2.7 ± 1	<0.001

Data were expressed as percent.
WC, waist circumference; HTN, hypertension; Hyper.TG, Hypertriglyceridemia; FPG, Fasting plasma glucose; HDL-C, High-density lipoprotein cholesterol.
[a] High WC: waist circumference ≥90 cm (men) or ≥80 cm (women) in Asian population; HTN: SBP > 130 mmHg, DBP > 85 mmHg or use of antihypertensive medications; Hyper.TG: fasting triglycerides > 150 mg/dL or lipid medications; High FPG: fasting plasma glucose ≥ 100 mg/dL or use of diabetes medications; Low HDL-C: HDL cholesterol < 40 mg/dL (men) or <50 mg/dL (women).
[b] Calculated as the number of positive criteria.
[c] P for trend across time.

Table 3
Adjusted odds ratios and 95% probability intervals for Metabolic Syndrome and number of Metabolic Syndrome positive criteria across quartiles of nuts intake.

	Nut quartiles				P for trend[b]	DIC	BP
	1st	2nd	3rd	4th			
MetS (yes/no)							
Model 1	1	0.74 (0.57–0.94)	0.89 (0.69–1.14)	0.82 (0.64–1.07)	0.38	4816	0.46
Model 2	1	0.76 (0.59–0.97)	0.94 (0.73–1.20)	0.83 (0.65–1.07)	0.43	4811	0.39
Model 3	1	0.76 (0.59–0.96)	0.89 (0.70–1.15)	0.77 (0.59–1)	0.14	4810	0.39
Model 4	1	0.99 (0.78–1.28)	1.06 (0.83–1.36)	0.95 (0.73–1.24)	0.87	4594	0.38
Severity of MetS[a]							
Model 1	1	0.75 (0.60–0.94)	0.89 (0.71–1.06)	0.88 (0.70–1.10)	0.26	7486	0.50
Model 2	1	0.78 (0.63–0.97)	0.93 (0.75–1.16)	0.90 (0.72–1.12)	0.25	7413	0.47
Model 3	1	0.77 (0.63–0.96)	0.88 (0.71–1.10)	0.82 (0.65–1.03)	0.03	7463	0.43
Model 4	1	0.96 (0.77–1.19)	1 (0.80–1.25)	0.98 (0.78–1.24)	0.27	7314	0.44

Data are expressed by odds ratio (95% probability interval). DIC, Deviance Information criteria; BP, Bayesian P-value.
Model 1: crude model. Model 2: adjusted by age, sex, SES, smoking status, total physical activity, medications for hypertension, diabetes and hyperlipidemia. Model 3: additionally, adjusted by total dietary score. Model 4: further adjusted for BMI.
[a] Calculated as the number of positive criteria.
[b] The nuts intake was used as a continuous variable in the models.

4. Discussion

This longitudinal study with three repeated measurements during 13 years of follow-up, evaluated the long-term association between nuts intake and both the risk and severity of MetS, were defined as the number of positive criteria, among the Iranian population. Nuts intake was negatively related to the long-term risk of developing MetS. In fact, the odds ratios for the risk and the severity of MetS decreased with the higher intake of nuts compared with the lower intake. In comparison with individuals in the lowest quartile, those in the second quartile of nuts intake were 24% less likely to have MetS, after adjusting for all considered confounders. Also, the severity of MetS had 23% reduction among participants in the second quartile compared with the first quartile. However, the association between nuts intake and the developing MetS was disappeared after additionally adjusted for BMI. It can mean the nuts reducing risk of MetS through changing BMI according to the result of other studies reported the inverse association of nut consumption and obesity [15,16,43].

Similar results were observed in other longitudinal studies examining the association between nuts intake and MetS. The National Health and Nutrition Examination Survey (NHANES) with five-year follow up, reported that higher intake of nuts such as pistachios, walnuts, hazelnuts, and almonds have decreased the risk of MetS components [17]. The result of the Seguimiento Universidad de Navarra (SUN) study in Spain suggested that women taking more than two servings of nuts per week had a lower risk of MetS compared with those consuming less [14]. The Tehran Lipid and Glucose Study (TLGS) reported that total nuts and walnut intake had a significant, negative relation with MetS incident [6]. The Several longitudinal studies have also indicated the protective effect of the Mediterranean or prudent dietary patterns included or supplemented with nuts on MetS [24–27]. The longitudinal ICS with three repeated measurements on diet and MetS information showed the long-term intake of healthy diet included nuts had a protective effect on the risk and severity of MetS [28].

These findings are consistent with a randomized clinical trial in which nuts intake has improved inflammation, oxidative stress, endothelial function, diabetes, insulin resistance, and hypertension and subsequently reducing the risk of obesity and CVD [19–23]. In addition, the inverse association of nuts and prevalence of MetS or its components has been reported in previous cross-sectional studies [15–18].

The effects of nuts can be explained by improving inflammation, endothelial function, and oxidative stress. These mechanisms can decrease the risk of insulin resistance and diabetes,

hypertension, abdominal obesity, and dyslipidemia as characteristics of MetS [22].

The beneficial effects of nuts on MetS and cardiovascular outcomes can be due to their healthy nutritional profile such as antioxidants, the protein of vegetable, vitamins, fiber, minerals including potassium and magnesium, high amounts of mono and polyunsaturated fatty acids, and multiple bioactive ingredients such as polyphenols and phytosterols [7–12].

To our knowledge, most of the previous surveys on the association between MetS and nuts intake were cross-sectional. Also, prospective studies were mostly limited to assess baseline measurement of nuts intake. Thus, our cohort study, with longitudinal measures of nuts intake and the outcome variables during 13-year follow-up conducted in a Middle Eastern country, could strengthen such findings. In this study, long follow-up excludes potential changes in individual diets. Nevertheless, some limitations exist in our study. Our FFQ was rather qualitative and not quantitative, by not taking into account the total energy intake. We used BMI as a surrogate for energy-adjusted intake. Further adjustment for physical activity was also done in our statistical analysis to consider the fact that likely more active individuals particularly those with manual work, have low BMI and high energy intakes [41]. We implied that dietary and outcome measurements were performed simultaneously, thus reverse causation bias can occur. Identifying causality requires an RCT.

In conclusion, our finding indicated the beneficial effect of nuts intake on the MetS risk and reducing the severity of MetS. The risk of cardiometabolic factors and MetS may be reduced by taking nuts in the diet.

Statement of authorship

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

Conflict of interest

The authors declare that they have no conflict of interest.

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