




## The relationship between dietary patterns, dietary quality index, and dietary inflammatory index with the risk of all types of cancer: Golestan cohort study

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### Abstract

**Background:** Dietary patterns and diet quality index (DQI) are widely discussed in relation with different health conditions and have recently been taken into consideration for all cancer types. Since chronic inflammation has been recognized as an important biologic risk factor for cancer occurrence, especially in epithelial tissues, proinflammatory or anti-inflammatory characteristics of diet has become the center of attention. In the present study, we aimed to identify whether a specific dietary pattern, Mediterranean dietary score (MDs), and dietary inflammatory index (DII) were associated with overall cancer risk in Iranian population.

**Methods:** This study was performed in the context of the Golestan cohort study. Participants with extreme daily energy intake or those who did not answer more than 30 question of the Food Frequency questionnaire (FFQ) were excluded. Dietary patterns, MDs, and DII were measured from FFQ. Age, sex, total energy, place of residence, smoking, wealth score, ethnicity, opiate use, BMI, education, marital status, and physical activity score were considered as confounding variables. Using Cox proportional hazards regression models, hazard ratios (HRs) and 95% confidence interval of cancer were estimated.

**Results:** HRs (95% CIs) of all cancers by quartiles of Western dietary pattern, DII, and MDs showed that the fourth quartile of the Western dietary pattern is attributed to 23% higher cancer risk (HRs: 1.23, CI: 1.09-1.40,  $P < 0.001$ , adjusted for age and sex) compared to the first quartile. It also remained significant after further adjustments (HRs = 1.20, CI: 1.06-1.36,  $P < 0.001$ ). There was a higher cancer risk in the fourth quartile of DII in comparison with the first quartile (HRs = 1.16, CI: 1.01-1.32,  $P$  trend  $< 0.001$ , adjusted for age and sex). The lower adherence to the Mediterranean dietary pattern also largely contributes to 27% higher cancer risk (HRs: 1.27, CI: 1.12-1.44),  $P$  trend  $< 0.001$ , adjusted for age and sex), which also remained remarkable after further adjustments ((HRs = 1.19, CI: 1.05-1.35,  $P$  trend  $< 0.001$ ).

**Conclusion:** Cancer is highly correlated to dietary intake and dietary patterns, such as the Western dietary pattern, while the Mediterranean diet score was inversely associated with cancer risk. Further investigations are required to get a broader insight into cancer determinants in population.

**Keywords:** Dietary Patterns, Dietary Quality Index, Dietary Inflammatory Index, Risk, Cancer, Golestan Cohort Study

**Conflicts of Interest:** None declared

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### ↑What is “already known” in this topic:

There is a large body of evidence on a correlation between dietary intakes and all types of cancer.

### →What this article adds:

The association between dietary patterns, diet quality index, and dietary inflammatory index with cancer incidence was assessed in the present article. The Western dietary pattern, inflammatory diet, and lower adherence to the Mediterranean dietary pattern contribute to 23%, 16%, and 27% higher cancer risk, respectively.

## Introduction

Cancer is one of the most important causes of death worldwide, accounting for 21% of the overall mortality (1), as it is estimated that its incidence will increase by 70% in the next 20 years (2). The number of new cancer cases reached 14.1 million in 2012 and is expected to rise to 23.6 million new cases in 2030 (3). Cancer etiology has been widely the center of attention to find major risk factors and consequently discover therapeutic modalities and cancer preventing intervention (4, 5). Since about one third of cancer deaths are associated with major behavioral and dietary risk factors like unhealthy diet or low fresh fruit and vegetable consumption, it is of great importance to further offset the effects of such risk factors (5).

Dietary patterns and diet quality index (DQI) are widely discussed in relation with different health conditions and have also been recently taken into consideration for all cancer types (6, 7). Dietary patterns assess the effects of whole diet, rather than individual nutrients or foods, enabling investigators to examine associations with overall diet (8). In the Dietary Patterns Methods Project, 4 indexes of diet (the Alternative Healthy Eating Index 2010 (AHEI-2010), the alternate Mediterranean diet score (aMED), and the Dietary Approaches to Stop Hypertension (DASH) were assessed in relation to colorectal cancer. Results of the mentioned study showed that all 4 diet quality indexes were inversely associated with colorectal cancer risk in both men and women, although the associations for the AHEI-2010 and aMED score after adjustment for potential confounding factors did not remain statistically significant in women (9).

A low-fat dietary pattern is reported to be associated with reduced pancreatic cancer incidence in women who were overweight or obese and fewer ovarian cancers among postmenopausal women (10, 11). Likewise, a specific dietary pattern that correlated with C-peptide concentrations was associated with an increase in colon cancer, especially among women who were overweight or sedentary (12). However, another survey found no association between a vegetarian pattern or a salty pattern and breast cancer (13). The Western dietary pattern also increased prostate cancer risk (14). Diet quality index is also composed of a combination of foods and/or nutrient components reflecting dietary guidelines and complexity of diet (15, 16). It seems that the Mediterranean dietary pattern as one of the dietary quality indices can reduce breast cancer risk as well as overall cancer risk (17, 18). Chronic inflammation has been also recognized as an important biologic risk factor for cancer occurrence, especially in epithelial tissues (19). As diet causes exposures to many different agents that can have proinflammatory or anti-inflammatory characteristics, its role in chronic inflammation and cancer development has been recently widely discussed, although data about the inflammatory potential of common diet in Iran is scarce or nonexistent. In 2014, an inflammatory index was developed to assess the inflammatory potential of an individual's diet (20). Some studies have shown an association between inflammatory potential of an individual's diet and incidence of different cancers like colorectal cancers (21-24), renal carcinoma

(25), esophageal squamous cell carcinoma (26, 27), hepatocellular (28), lung (29), prostate (30-32), and breast cancer (33, 34).

In the present study, we aimed to identify whether a specific dietary patterns, MDs and dietary inflammatory index, were associated with overall cancer risk in an Iranian population.

## Methods

### Study population

This study is a part of the Golestan cohort study done in Golestan province located in the northeast of Iran. Golestan cohort study recruited about 50 000 healthy persons aged between 40 and 75 years during 2004 and 2008 to investigate the etiology of esophageal cancer; all details are published elsewhere (35). Some participants were excluded from the study because of extreme daily energy intake, defined as >99th percentile or less than the first percentile, or with missed >30 responses on the FFQ. The ethical review committee of the Digestive Diseases Research Institute approved the study protocol.

### Data collection and measures

Characteristics of the participants, including age, smoking status, ethnicity, education levels, history of diseases physical activity levels, and family history of cancer, were obtained through face-to-face interviews using a general questionnaire at the beginning of the study. Weight was measured using digital scales, while participants were minimally clothed, without shoes to the nearest 100g. Height was measured using a nonstretchable tape meter in a standing position without shoes to the nearest 0.5 cm. The body mass index (BMI) was calculated as weight (kg) divided by square of the height (m<sup>2</sup>). Since physical activity at work is considered to be mostly staple, it was used to calculate a physical activity score (36). Using household appliances, vehicles, and other variables associated with wealth through multiple correspondence analysis wealth score was estimated (37). Marital status was considered as single or married. Because the number of divorced or widowed individuals was small, they were categorized in a single category.

### Dietary intake

The dietary intake was measured using a validated 116-item Food Frequency Questionnaire (FFQ), which was designed especially for GCS population (38). Participants were asked about their intake frequency for each food item consumed during the past year on a daily, weekly, or monthly basis; portion sizes of consumed foods reported in household measures were then converted to grams. To analyze food items in terms of the energy and nutrient intake of participants, the Iranian Food Composition Table and the food composition tables (FCT) of the United States Department of Agriculture (USDA) were used.

### Dietary pattern

In order to determine dietary patterns, the principle

component analysis (PCA) was applied based on dietary information collected from the 18 food groups (Table 1) based on the similarity in their nutrient contents. Data of food groups were standardized and then considering  $\pm 4SD$ , data were truncated. Skewed data were normalized using logarithm method, and then data were energy adjusted by the residual methods. The factors were rotated with varimax rotation. Considering Eigen values  $>1$ , the scree plot, and the interpretability of the factors, 3 patterns were identified. Items which have absolute correlation  $\geq 0.2$  with that factor were considered to load on a factor and retained in the calculation of the dietary pattern score (39). The Kaiser-Mayer-Olkin statistic was 0.88, which indicate a good appropriateness of factor analysis. This statistic considers a measure of sampling adequacy. To evaluate the suitability of the correlation matrix for factor analysis, Bartlett's test of sphericity was used; P value for Bartlett's test of sphericity was  $< 0.001$ . Factor scores of the participants were calculated using sum of multiplying the intake of the standardized food groups by their respective factor loadings on each pattern. The factor loading of

the 3 dietary patterns extracted by factor analysis is presented in Table 2.

Among the 3 extracted dietary patterns, only the Western dietary pattern, which correlated with cancer risk, was reported.

#### Mediterranean diet score (MDs)

The Mediterranean diet score was computed according to data obtained from FFQ. Seven components (saturated fatty acids, cholesterol, meat, olive oil, fish, cereals, and vegetables + fruits) were assessed in this index and score of 0, 1, or 2 were assigned to the daily intake of each of the mentioned component. A total score ranged between 0 and 14, with lower scores indicating a high quality of diet and better adherence to the Mediterranean dietary pattern (40).

#### Dietary inflammatory index

To calculate the dietary inflammatory index, we used 31 food items that were available in our food composition database and we also applied the standardized method

Table 1. Food grouping used in the dietary pattern analysis

Food Group	Food items
1. Refined grains	White bread (Lavash, baguettes), noodles, pasta, rice, toasted bread, sweet bread, white flour, biscuits
2. Fast foods	Sausage, Hamburger, sausages
3. Sour-Salty snacks	Salt, Pickle, Vinegar
4. Egg	Egg (all preparations)
5. Vegetables	All green leafy, cruciferous, yellow, tomato, and other vegetables
6. Whole grains	All whole and dark breads, barley, wheat, wheat germ, shredded wheat/barely, corn, biscuits prepared with whole grains
7. Fruits	All fruit and natural fruit juices
8. Fish	All fishes, canned tuna fish, (all preparations)
9. Fish processed	canned tuna fish, smoked fish, salted fish
10. poultry	Every part and all preparation
11. High- and low-fat dairy products	High-fat milk and yogurt, chocolate milk, creamy yogurt, creamy cheese, ice cream, low-fat milk and yogurt, cheese
12. Oils	All vegetable oils, Liquid and Solid oils, animal fats
13. Sweets	Sugar, honey, All cakes, confections, chocolates, cookies, all biscuits, desserts
14. Red meats	Beef, lamb, minced meat
15. Organ meats	Liver, brain, and the other organ meats
16. Nuts and seeds	All nuts and seeds (raw or roasted)
17. Legumes	All kinds of beans, peas, lentils, soy
18. Olives	Olives, Olive oil

Table 2. Factor loading of 3 dietary patterns extracted by factor analysis

Food Groups	Healthy dietary pattern	Western dietary pattern	Mixed dietary pattern
Fruit and dried fruit	0.662 <sup>a</sup>		
Refined grains	-0.597		
Olive oil	0.551		
High- and low-fat dairy products	0.452		
Poultry and fish	0.327		
Liquid oils except olive oil	0.240		
Canned products	0.279		
Carbonated drinks		0.677	
Fast foods		0.603	
Salty snacks		0.573	
Mayonnaise		0.581	
Organ meats		0.311	
Legumes			0.635
potatoes			0.639
Egg			0.512
Red meats			0.477
Tea			0.252
Percentage of variance explained <sup>b</sup>	11	10	7

<sup>a</sup>Values are factor loading of dietary patterns (n=2141). Factor loading  $\leq 0.2$  are not shown.

<sup>b</sup>Eigen value  $>1$ .

provided by Shivappa (9). These food items were vitamin B12, vitamin B6,  $\beta$ -carotene, caffeine, carbohydrate, cholesterol, energy, fat, fiber, folic acid, iron, magnesium, niacin, protein, riboflavin, selenium, thiamin, vitamin A, vitamin C, vitamin D, zinc, trans fatty acid, saturated fat acids (SFA), monounsaturated fat acids (MUFA), polyunsaturated fatty acids (PUFA), garlic, onion, saffron, turmeric, black tea, and pepper. The calculation method has been described elsewhere in detail (9). Briefly, a standard mean for each food item from the representative world database was subtracted from the daily intake and divided by its standard deviation to generate Z scores. For minimizing the effect of right skewing, the percentile value was converted to percentile score using SPSS and these values were divided by 100 to calculate the scoring of 0-1. Also, to generate a centered percentile score on 0 (null) and bounded between -1 (maximally anti-inflammatory) and +1 (maximally pro-inflammatory), each percentile score is doubled and then '1' is subtracted. Then, these values were multiplied by the respective overall food parameter-specific inflammatory effect score to obtain the 'food parameter specific DII score'. Finally, all of the food parameter-specific DII scores are summed to generate the overall DII score for an individual.

### Statistical analysis

Using Cox proportional hazards regression models, HRs and 95% CIs were estimated. Using Aalen plots and the Schoenfeld residuals test, the proportional hazards assumption was checked. Age was used as the underlying time metric. All possible confounders were investigated; namely, age, sex, total energy, place of residence, smoking, wealth score, ethnicity, opiate use, BMI, education, marital status, and physical activity score. The model was not adjusted for alcohol drinking, as only few participants reported drinking alcohol, and it is not deemed to be a risk

factor in the corresponding area (41).

Multivariate HRs were reported within quartiles where the lowest quartile was considered as the reference category. For linear trend tests, the median value of each quartile was used. We also conducted stratified analyses by age, sex, BMI, ethnicity, and residence area. Statistical analyses were performed by using STATA software (version 12; StataCorp). Reported P values are 2-sided.

### Results

Among the participants, 49 940 were included in the final analysis (21 207 men and 28 733 women). During a median follow-up time of 10.1 years (IQR: 9.16-11.18 y), 1932 cases were diagnosed with any type of cancer. Baseline characteristics are shown according to the quartile of the dietary pattern, Med-DQI, and DII separately (Tables 3, 4, and 5). A higher adherence to the Western dietary pattern was associated with increased energy intake and smoking, and lower wealth score in the fifth category and also lower education level. Towards higher quartiles of MDs representing lower adherence to the Mediterranean dietary pattern, lower energy intake and BMI, and decreased wealth score in most categories were indicated. Upper quartiles of DII were also associated with lower BMI and energy intake and also lower wealth score in higher categories.

Table 6 indicates HRs (95% CIs) of all cancers, by quartiles of the Western dietary pattern, DII, and MDs. The fourth quartile of the Western dietary pattern is attributed to 23% higher cancer risk (HRs: 1.23, CI: 1.09-1.40,  $P < 0.001$ , adjusted for age and sex) compared to the first quartile. It also remained significant after further adjustments (HRs = 1.20, CI: 1.06-1.36,  $P < 0.001$ ). There was a higher cancer risk in the fourth quartile of DII in comparison with the first quartile (HRs = 1.16, CI: 1.01-1.32,  $P$  trend  $< 0.001$ , adjusted for age and sex). Lower

Table 3. Baseline characteristics of participants by quartiles of the Western dietary pattern<sup>1</sup>

Quartile Variable	Q1	Q2	Q3	Q4
Western Dietary Pattern score	-0.99±1.36	0.14±0.15	1.13±0.46	6.46±10.54
Male sex, n (%)	5179 (41.7)	5185 (43.1)	5327 (43.5)	5114 (41.7)
Age (y)	52.38±9.15	51.90±8.81	51.91±8.91	52.24±9.16
Energy (kcal)	2124±590	2241±601	2240±627	2141±1826
BMI (kg/m <sup>2</sup> )	26.60±5.45	26.82±5.40	26.78±5.43	26.51±5.49
Smoker, n (%)	2731 (22)	2489 (20.7)	2647 (21.6)	2802 (22.8)
Wealth score <sup>3</sup> , n (%)				
1	2620 (21.10)	2345 (19.5)	2339 (19.1)	3007 (24.5)
2	2283 (18.4)	2238 (18.6)	2229 (18.2)	2296 (18.7)
3	2618 (21.1)	2774 (23.1)	2738 (22.3)	2559 (20.9)
4	2295 (18.5)	2434 (20.2)	2446 (20)	2176 (17.7)
5	2599 (20.9)	2231 (18.6)	2503 (20.4)	2232 (18.2)
Physical activity score, n (%)				
Low	4414 (35.6)	4118 (34.3)	4346 (35.5)	4448 (36.3)
Intermediate	4086 (32.9)	3707 (30.8)	3809 (31.1)	3848 (31.4)
High	3892 (31.3)	4176 (34.7)	4069 (33.2)	3937 (32.1)
Rural place of residence, n (%)	10335 (83.2)	9966 (82.9)	10075 (82.2)	10080 (82.2)
Turkmen ethnicity, n (%)	8157 (65.7)	9739 (81)	9393 (76.6)	9026 (73.6)
Opium user, n (%)	2033 (16.4)	2010 (16.7)	2057 (16.8)	2222 (18.1)
Marital status, single, n (%)	1582 (12.7)	1307 (10.9)	1382 (11.3)	1684 (13.7)
No formal education, n (%)	8782 (70.7)	8520 (70.9)	8435 (68.8)	8561 (69.8)

<sup>1</sup> n = 49940

<sup>2</sup> Mean ± SD (all such values)

<sup>3</sup> Wealth score was estimated through multiple correspondence analyses on the basis of household appliances, vehicles, and other variables associated with wealth

Table 4. Baseline characteristics of subjects by quartiles of the Mediterranean diet score (MDs)<sup>1</sup>

Quartile Variable	Q1	Q2	Q3	Q4
MD score	2.48±0.44	3.35±0.18	4.03±0.23	6.11±2.09
Male sex, n (%)	7399 (60.5)	5846 (47.6)	4586 (37.4)	2975 (24.4)
Age (y)	51.63±8.71	51.41±8.75	51.78 ± 8.85	53.62±9.55
Energy (kcal)	2922±1781	2335±265.58	1998 ± 211.23	1489±301.73
BMI (kg/m <sup>2</sup> )	27.12 ± 5.27	26.83±5.33	26.67± 5.41	26.10±5.72
Smoker, n (%)	3428 (28)	2872 (23.4)	2336 (19.1)	2034 (16.7)
Wealth score <sup>3</sup> , n (%)				
1	2181 (17.8)	2404 (19.6)	2563 (20.9)	3164 (25.9)
2	1912 (15.6)	2245 (18.3)	2322 (19)	2569 (21)
3	2363 (19.3)	2767 (22.5)	2872 (23.4)	2689 (22)
4	2423 (19.8)	2512 (20.5)	2353 (19.2)	2064 (16.9)
5	3344 (27.4)	2353 (19.2)	2142 (17.5)	1726 (14.1)
Physical activity score, n (%)				
Low	4954 (40.5)	4275 (32.4)	3965 (33.1)	4135 (33.9)
Intermediate	3489 (28.5)	3977 (32.5)	7399 (31.5)	4205 (34.4)
High	3750 (30.7)	4285 (35)	8267 (35.2)	3842 (31.5)
Rural place of residence, n (%)	9319 (76.2)	9931 (80.9)	10412 (85)	10799 (88.4)
Turkmen ethnicity, n (%)	9243 (75.6)	9332 (76)	9193 (75)	8550 (70)
Opium user, n (%)	2247 (18.4)	2053 (16.7)	1881 (15.4)	2141 (17.5)
Marital status, single, n (%)	976 (8)	1155 (9.4)	1505 (12.3)	2319 (19)
No formal education, n (%)	7050 (57.7)	8257 (67.2)	8997 (73.4)	10000 (81.9)

<sup>1</sup> n = 49940<sup>2</sup> Mean ± SD (all such values)<sup>3</sup> Wealth score was estimated through multiple correspondence analysis on the basis of household appliances, vehicles, and other variables associated with wealthTable 5. Baseline characteristics of participants in the Golestan cohort study by quartiles of dietary inflammatory index (DII)<sup>1</sup>

Quartile Variable	Q1	Q2	Q3	Q4
DII score	-1.05±0.32	-0.32±0.18	0.39±0.24	1.90±1.20
Male sex, n (%)	6785 (55.5)	5999 (48.9)	4783 (39.2)	3248 (26.4)
Age (y)	51.32±8.61	51.51±8.74	52.07±9	53.53±9.52
Energy (kcal)	2621±560	2488±1688	2072±691	1565±360
BMI (kg/m <sup>2</sup> )	27.67±5.26	26.80±5.35	26.47±5.41	25.80±5.60
Smoker, n (%)	3206 (26.2)	2910 (23.7)	2546 (20.9)	2013 (16.4)
Wealth score <sup>3</sup> , n (%)				
1	1375 (11.2)	2435 (19.9)	2765 (22.7)	3742 (30.4)
2	1541 (12.6)	2226 (18.2)	2460 (20.2)	2827 (23)
3	2218 (18.1)	2777 (22.6)	2895 (23.7)	2802 (22.8)
4	2752 (22.5)	2472 (20.2)	2274 (18.6)	1860 (15.1)
5	4346 (35.5)	2353 (19.2)	1802 (14.8)	1066 (8.7)
Physical activity score, n (%)				
Low	4770 (39)	4297 (35)	3978 (32.6)	4293 (34.9)
Intermediate	3631 (29.7)	3756 (30.6)	3938 (32.3)	4131 (33.6)
High	3798 (31)	4180 (34.1)	4260 (34.9)	3844 (31.3)
Rural place of residence, n (%)	9462 (77.4)	9893 (80.7)	10239 (84)	10884 (88.5)
Turkmen ethnicity, n (%)	7391 (60.4)	9423 (76.8)	9752 (80)	9772 (79.5)
Opium user, n (%)	2007 (16.4)	2072 (16.9)	2104 (17.3)	2146 (17.5)
Marital status, single, n (%)	1053 (8.6)	1175 (9.6)	1500 (12.3)	2230 (18.1)
No formal education, n (%)	6123 (50.1)	8317 (67.8)	9246 (75.8)	10632 (86.5)

<sup>1</sup> n = 49940<sup>2</sup> Mean ± SD (all such values)<sup>3</sup> Wealth score was estimated through multiple correspondence analysis on the basis of household appliances, vehicles, and other variables associated with wealth

adherence to the Mediterranean dietary pattern also largely contributes to 27% higher cancer risk (HRs: 1.27, CI: 1.12-1.44), P trend < 0.001, adjusted for age and sex), it also remained remarkable after further adjustments (HRs = 1.19, CI: 1.05-1.35, P trend < 0.001).

## Discussion

In the present population-based survey, cancer incidence was associated with higher adherence to the Western dietary pattern, higher DII, and lower adherence to the Mediterranean diet. Apart from the results referring to DII, all findings remained significant after adjustment for all confounding variables.

Among the 3 dietary patterns extracted from the dietary

intakes of the participants, the Western dietary pattern was associated with the risk of cancer. This dietary pattern was rich in carbonated drinks, fast foods, salty snacks, and mayonnaise. It was reported to increase cancer risk by 20% in this study. Red meat and tea were classified under mixed dietary pattern. Different methods of red meat processing such as grilling can be effective in making carcinogens such as heterocyclic amines. On the other hand, hot tea consumption can also contribute to esophageal cancer.

Diet is widely discussed as a modifiable determinant for cancer, as healthy dietary patterns seem to be related to decreased risk of colon and breast cancer and unhealthy dietary patterns can lead to increased risk of colon cancer (42, 43). However, it can no longer be generalized about

Table 6. Hazard ratios (95% CIs) of all cancer by quartiles of the Western dietary pattern, DII, and MDS score

Quartile Variable	Q1	Q2	Q3	Q4	P-trend
Western Dietary pattern					
Score	-0.55 (0.91) <sup>1</sup>	0.11 (0.25)	1.06 (0.78)	4.26 (3.94)	
Person-years	123768	120700	122731	122673	
Cases (n)	448	426	482	532	
HR (95% CI) <sup>2</sup>	1	1.01 (0.88-1.15)	1.12 (0.99-1.28)	1.23 (1.09-1.40)	<0.001
HR (95% CI) <sup>3</sup>	1	0.99 (0.86-1.13)	1.11 (0.98-1.26)	1.20 (1.06-1.36)	<0.001
DII					
Score	-0.98 (0.44)	-0.33 (0.32)	0.37 (0.42)	1.58 (1.11)	
Person-years	125750	123574	121412	119425	
Cases (n)	444	435	484	527	
HR (95% CI) <sup>2</sup>	1	0.98 (0.86-1.12)	1.08 (0.95-1.23)	1.16 (1.01-1.32)	<0.001
HR (95% CI) <sup>3</sup>	1	0.92 (0.80-1.05)	0.99 (0.87-1.14)	1.03 (0.89-1.19)	<0.001
MDS					
Score	2.59 (0.58)	3.36 (0.31)	4.01 (0.40)	5.49 (1.73)	
Person-years	125632	123662	234095	117300	
Cases (n)	468	463	878	524	
HR (95% CI) <sup>2</sup>	1	1.04 (0.91-1.18)	1.11 (1.00-1.24)	1.27 (1.12-1.44)	<0.001
HR (95% CI) <sup>3</sup>	1	1.02 (0.90-1.17)	1.07 (0.95-1.19)	1.19 (1.05-1.35)	<0.001

<sup>1</sup>Median (IQR)<sup>2</sup>Adjusted for age (y) and sex<sup>3</sup>Adjusted for age (y), sex, total energy (kcal/d), place of residence (urban or rural), smoking (never or ever), wealth score (1-5), ethnicity (non-Turkmen or Turkmen), opiate use (never or ever), BMI (kg/m<sup>2</sup>), education (illiterate or formal education), marital status (single or married), and physical activity score (categorical)

different cancer types and varied target populations, since these results are inconsistent with some of previous studies (44-46). There may not be correlations between unhealthy dietary pattern and risk of upper digestive tract, pancreatic, ovarian, endometrial, and prostatic cancers based on case-control studies (44, 47). On the other hand, it is also likely that dietary parameters can directly or indirectly affect cancer incidence. A balanced ratio of fatty acids, the high fiber content, and the substantial amounts of antioxidant compounds result in suppressing multiple cancer-related biological pathways, including carcinogen bio activation, cell signaling, cell cycle regulation, angiogenesis, and inflammation (2). Altered energy imbalance, excess body weight, adverse homeostasis alterations are also the indirect consequences of improper eating habits. Moreover, unhealthy dietary patterns mostly contain salt, N-nitros compounds, heterocyclic amines, heme iron, and polycyclic aromatic hydrocarbons, which are deemed to be responsible for the carcinogenic effects (48). Accordingly, a low-fat dietary pattern is proposed to reduce the incidence of ovarian cancer among postmenopausal women and pancreatic cancer incidence in women who were overweight or obese (10, 11).

In the model by which we calculated MDs, a higher score is associated with lower adherence to the Mediterranean diet; thus, across the upper quartiles of MDs, 19% increase in cancer risk is reported. In other word, the more participants were adhered to the Mediterranean diet, the less cancer risk they were exposed to. Adherence to MDs is considered as a remarkable protective factor for cancer incidence, decreasing the risk of almost all cancers (18).

The Mediterranean dietary pattern has a protective role for breast, female genital tract, urinary tract, and a few other epithelial neoplasms (49). Various antioxidants and other micronutrients provided by the Mediterranean diet has an inverse relationship with cancer risk, but the main components responsible for the favorable effect of a diet rich in vegetables and fruit remain undefined. Fish is an-

other useful component of this dietary pattern (50). On the contrary, red meat consumption is related to several common neoplasms. Another component of the Mediterranean diet that has a preventive role in cancer is whole-grain foods that are related to a reduced risk of several types of cancer, particularly of the upper digestive tract. This may be due to an effective role of fiber. However, refined grain intake and, consequently, glycaemic load and glycaemic index were associated with increased risk of different types of cancer, including breast and colorectal, among others (51).

There was also a suggestive positive association between a higher DII score and cancer risk among the participants. Diet seems to be closely related to chronic inflammation status (52, 53). Some studies have shown an association between inflammatory potential of an individual's diet and incidence of different cancers like colorectal cancers (16-19), renal carcinoma (20), esophageal squamous cell carcinoma (21, 22), hepatocellular (23), lung (24), prostate (25-27), and breast cancer (28, 29). Oxidative stress and reduced antioxidant defense system are also associated with cell injury and aging process in cellular level, which play a role in inflammatory and degenerative diseases and abnormal cell growth (30). In such context, foods with anti-inflammatory effects can play a key role in protection against reactive oxygen species and control process of aging, apoptosis, tumor cell growth, and cell injury (31).

The main strength of this study is the large sample size, which helps to generalize the results. This study had several limitations that need to be considered. Since diet is a very complex and potentially modifiable exposure, it is very difficult to elicit information on dietary intake. In addition, human diet is a potentially modifiable exposure; as a result, it is difficult to attribute the etiology of cancer to a single nutrient. Thus, in the present study, dietary patterns were preferred to be assessed. On the other hand, the Food Frequency questionnaire (FFQ) has been widely

used to capture habitual dietary intake, while its accuracy still remains a concern.

### Conclusion

Our findings suggest that avoiding the Western dietary patterns and diet with inflammatory potential and adherence to the Mediterranean diet pattern may be helpful in reducing the chances of cancer incidence. Further investigations are required to obtain a broader insight into cancer determinants in Iranian populations.

### Conflict of Interests

The authors declare that they have no competing interests.

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