Diet Quality and Dietary Acid Load in Relation to Cardiovascular Disease Mortality: Results From Fasa PERSIAN Cohort Study

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Abstract

Background: Dietary intake is a determining factor in the morbidity and the mortality of chronic disorders. However, not many documents have investigated this relationship. The aim of this study was to evaluate the associations of the Dietary Inflammatory Index (DII), Alternative healthy eating index (AHEI), Mediterranean dietary score (MDS), DASH score, and dietary acid load with cardiovascular disease (CVD) mortality.

Method: 2158 CVD patients (mean age of 54.73 ± 8.62 years) from the Fasa Cohort Study, Iran participated in the current study. Diet quality indices including DII, AHEI, MDS, DASH, and dietary acid load (NEAP score) were computed using a validated 125-item Food Frequency Questionnaire (FFQ). Cox regression analyses were used to determine HRs and 95% CIs.

Results: During a follow-up of 3 years, we documented 59 CVD deaths. After adjusting for relevant confounders (age, gender, smoking, alcohol intake, physical activity, family history of CVD, and HTN) in the final model, we found that higher DII scores and dietary acid load were significantly related to increased mortality due to CVD (HR =1.11; 95% CI =1.01-1.24 and HR =1.02; 95% CI =1.01-1.03). However, the DASH score was insignificantly associated with decreased CVD mortality by 20.4% (HR =0.79; 95% CI =0.57-1.09). There was no significant relationship among AHEI score, MDS, and CVD mortality.

Conclusions: This study showed that increasing dietary acidity and the use of inflammatory food compounds could contribute to CVD mortality. Also, adherence to the DASH diet may be associated with a reduced CVD mortality.

Introduction

Cardiovascular disease (CVD) is referred to as a group of related disorders that include hypertension, atherosclerosis, ischemic heart disease, peripheral arterial disease, and heart failure. The prevalence of CVD and its mortality have been 422.7 million cases and 17.9 million, during a year in the world, respectively.(1, 2) Evidence has shown that age, genetics, ethnicity, gender, hypertension, smoking history, abdominal obesity, physical inactivity, and poor diet are the risk factors of CVD; nevertheless, by identifying these risk factors in individuals, we can adopt an appropriate strategy for treatment and prevention.(1) Among the risk factors, dietary modification was an important approach for the prevention and management of CVD and its mortality. A diet with excessive sodium, saturated fatty acids, cholesterol, refined grains, red and processed meat, and alcohol could increase the risk of CVD and its mortality, while consumption of fruits, vegetables, legumes, seafood, nuts, whole grains, and unsaturated fatty acids is shown to be linked to reduced mortality of CVD.(3) Evidence suggested that Mediterranean dietary patterns and the dietary approach to stop hypertension (DASH) diet could reverse the CVD progression.(4) Previous documents for the control and management of CVD focused mainly on single micronutrients or food items. However, these days, instead of evaluating single nutrients or groups of

food, analysis of dietary pattern and dietary indices considers interactions and dependencies among nutrients and provides appropriate strategies for chronic disease management and prevention.(3)

The quality of the diet can be assessed by Alternative Healthy Eating Index (AHEI), Mediterranean diet score (MED), and DASH scores indices. According to a meta-analysis, the higher the score of these indices was significantly inversely associated with CVD progression and all reason mortality. (3, 5)

Recently, studies introduce acid-base dietary imbalance as a risk factor for chronic diseases, so that a higher dietary acid load increases the incidence of CVD, hypertension, and related mortality. (6) Consuming fewer amounts of fruits and vegetables simultaneously with excessive eating red and processed meat can reduce of the amount of diet and increase its acid load.(7) The dietary acid load could be elevated using potential renal acid load (PRAL), dietary acid load (DAL), and net endogenous acid production (NEAP). Higher scores of PRAL, DAL, and NEAP scores show more acid-loading potential. (7)

Evidence has demonstrated that inflammation is involved in the stages of atherosclerosis leads to plaque rupture and thrombosis which increase the probability of CVD mortality. In this regard, a diet rich in anti-inflammatory ingredients plays an important role in reducing the severity and consequence of inflammatory chronic disease the same as CVDs and this mortality. For evaluating the inflammatory and anti-inflammatory strength of a diet, a dietary inflammatory index (DII) is recommended. A higher score of DII, indicating a higher inflammatory diet, has been related to the risk of CVD and its mortality.(8, 9)

The recent study aimed to investigate the prospective relationships of the DII, MDS, AHEI, DASH score, and Dietary Acid Load with the mortality of CVD in the context of the epidemiologic Persian cohort study.

Methods

Study population

The present study included 1622 women and 536 men with cardiovascular diseases who participated in the Fasa PERSIAN Cohort as a branch of the Prospective Epidemiological Research Study in Iran. It was conducted during November 2014 and June 2019. In this cohort study, 10135 individuals aged 35 to 70 years who were not physically or mentally disabled, and lived in Sheshdeh, a district of Fasa for more than 9 months each year participated. (10) 2222 subjects were excluded from the study due to incomplete data on the intake of diet and mortality status as well as reports of abnormal energy intake (Less than 800 kcal and more than 4200 kcal). Finally, a total of 2158 participants with CVD took part in the current research. Information on demographic, behavioral, anthropometric data, medical history, and intake of foods was assessed through questionnaires biennially in the cohort study; likewise, mortality status and the cause of mortality were determined during the annual follow-up.(10) This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving patients were approved by the Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran (code: IR.SUMS.REC.1399.1116). Written informed consent was provided from all patients.

Dietary intake assessment and indices

The usual dietary intake of patients was assessed using a validated 125-item Food Frequency Questionnaire (FFQ) which was modified by the Iranian food culture.(10, 11) An expert nutritionist in a face-to-face interview registered the amount of food in the last year. Nutritionist IV software (version 7.0) was used to determine the energy and nutrient contents of foods.(10)

Alternative Healthy Eating Index-2010 (AHEI-2010)

Kennedy et al. designed the AHEI index to assess the quality of the diet. This index includes 11 components and the individuals are scored based on the consumption of these items. Fruits, vegetables, whole grains, nuts and legumes, DHA and EPA, and polyunsaturated fatty acids are positive components, while sweetened beverages, red and processed meats, trans-fatty acids, and sodium are the negative components; alcohol is the moderate component. For calculating, first, we categorized the individuals based on consumption deciles and then inverted the negative component decile score and finally summed the total score. The total score was from 9 to 81. A higher score of AHEI indicates a healthy diet.

DASH Score

There are different methods for calculating the DASH diet score. In this study, Mellen's DASH Index was applied. Its components included fiber, calcium, magnesium, cholesterol, sodium, potassium, protein, total fat, and saturated fat. The score was considered 1 point for the goal consumption and 0.5 for the intermediate intakes. The total score ranged from 0 to 9. A higher score indicates more adherence to the DASH diet.

Mediterranean dietary score (MDS)

In this study, we used MEDI-LITE scoring for this pattern, which was described by Francesco Sophie et al. This score focuses on nine components (vegetable, fruit, fish, grains, meat and meat products, dairy products, legumes, alcohol, and olive oil). Higher consumption of cereals, legumes, fruit, fish, and vegetables is scored 2 points, intermediate consumption 1 points, lower intake of them 0 points. The scoring of dairy products, processed meat, and meat was opposite of the previous groups. Medium consumption of alcohol was scored 2 points, the lowest consumption 1 point, and the highest intake 0 points. The final score was between 0 and 18 points. Higher scores indicate greater adherence to the MDS.

Dietary Inflammatory Index (DII)

we computed the DII score based on 30 groups of food including energy, fat, trans-fat, cholesterol, carbohydrate, protein, saturated fat, vitamin B12, iron, MUFA, PUFA, vitamin B6, fiber, vitamin B9, niacin, thiamin, riboflavin, vitamin A, magnesium, vitamin C, vitamin E, vitamin D, β -carotene, garlic, tea, onion, zinc, selenium, and caffeine. Consumption of groups such as eugenol, turmeric, saffron, ginger, pepper, rosemary, polyphenols, and anthocyanin was not available for the calculation of this index. First, the

energy intake of the participants was adjusted based on 1000 kcal. Then, to calculate DII, we subtracted the dietary parameters from global average and divided it by the “global standard deviation” to get a Z score. The Z-score values were then converted to percentiles. The percentile values were then multiplied by 2 minus 1. Finally, the scores obtained from each of the 30 parameters were multiplied by the overall inflammatory score; then, we summed up all food items to calculate the total DII score.

Dietary Acid Load

We constructed acid load of the diet based on the intake of several nutrients using three different methods: PRAL (mEq/d) = (protein [g/d] × 0.49) + (Phosphorous [mg/d] × 0.037) – (potassium [mg/d] × 0.021) – (Calcium [mg/d] × 0.013) – (magnesium [mg/d] × 0.026), NEAP (mEq/day) = (54.5 × protein [g/d]/potassium [mEq/d]) - 10.2 and DAL (mEq/ day) = PRAL + (body surface area [m²] × 41 [mEq/ day]/1.73 m²). Du Bois formula: $height^{0.725} \times weight^{0.425} \times 0.00718$ was used for computing the surface of the body. Acid load score obtained from these three methods was used for statistical analysis. (16)

Assessment of other variables

Cardiovascular patients were followed up clinically during a 3-year period. They were Identified based on previous medical history, Electrocardiography, Laboratory sampling, Validated screening questionnaires, and physical exams. the International Physical Activity Questionnaire (IPAQ) was applied for Physical activity. Using a digital scale (tanita BC-418, tanita corp, japan), we recorded the height and weight. Body mass index (BMI) was then calculated by weight (kg)/height (m)². Waist circumference was measured with a precision of 0.1cm. The medical history and lifestyle factors that are associated with CVD risk were recorded.(10)

Outcome assessment

In this study, our outcome was cardiovascular mortality; based on the 10th edition of the International Classification of Diseases (ICD), deaths due to the following diseases are considered CVD mortality: hypertension (ICD I10-I15), ischemic heart disease (ICD I20-I25), peripheral vascular disease (ICD I70-I89), stroke (ICD I60-I69), and Pulmonary-heart disease (ICD I26-I28). The patients' CVD mortality was followed for 3 years.

Statistical analysis

SPSS software version 21 was used to analyze the data. Quantitative variables are reported as mean ± standard error and qualitative data are presented as frequency (percentage). The normality of the distribution of variables was evaluated using the Kolmogorov-Smirnov test. Mann-Whitney U tests and Chi-Square tests were used to compare quantitative and qualitative data among the participants based on gender, respectively. A Cox regression analysis was used to assess the relationship among the four dietary quality indices (DII, DASH score, MDS, and AHEI), dietary acid load, and CVD mortality. The outcome was defined as mortality, the temporal factor was time to the event, and exposure was one of

the dietary indexes. We did not adjust for any covariates in the first Model (basic Model). The second model was adjusted for covariates including age, gender, smoking, alcohol intake, level of physical activity, family history of CVD, and history of HTN. The third model was adjusted by total energy, waist to hip ratio (WHR), BMI, weight, DBP, SBP, TG, cholesterol, LDL, and HDL. Finally, the model was adjusted with all the components of models 2 and 3. The Hazard ratio (AR) and 95% confidence interval (CI) were presented to show the strength of the relationship between dietary quality indices including DII, AHEI, MDS and DASH score, and dietary acid load and the CVD mortality. P values of <0.05 were considered significant.

Results

2158 individuals (24.8% male and 75.2% female), with a mean age of 54.73 ± 8.62 years participated in this study. During a 3-year follow-up of the present study participants, 59 deaths (30 males and 29 females) due to CVD got recorded.

Table 1 displays the basic characteristics of the study patients. As shown in this Table, the mean age, weight, and serum cholesterol were significantly higher in men with CVDs compared to women ($P = <0.05$), but their BMI, WHR, and the serum level of TG, HDL, and LDL were significantly lower ($P = <0.05$). Based on Table 1, the frequency distribution of the participants in terms of the history of hypertension was significantly higher in a woman with CVDs compared to men. ($P = <0.05$). However, the frequency distribution of the history of alcohol consumption and active smoking was significantly lower ($P = <0.05$). Table 1 also shows that 5.6 and 1.8 percent of men and women with CVDs died due to cardiovascular events, which is significantly higher in men ($P = <0.05$). (Table 1)

Table 1
Distribution of baseline variables in men and women

	Total	Men (n=536)	Women (n=1622)	P_value
Age (year)	54.73 ± 8.62	57.04 ± 8.81	54.41 ± 9.02	<0.0001
Weight (Kg)	67.76 ± 1.32	71.13 ± 13.47	66.67 ± 12.83	<0.0001
BMI (kg/m ²)	27.09 ± 4.94	25.30 ± 4.28	27.7 ± 4.96	<0.0001
WHR	0.96 ± 0.06	0.94 ± 0.06	0.96 ± 0.06	<0.0001
Physical activity (MET)	38.45 ± 8.38	40.68 ± 12.47	37.7 ± 6.3	0.65
DBP (mmHg)	79.97 ± 13	79.65 ± 13.83	80.07 ± 12.73	0.63
SBP (mmHg)	123.04 ± 21.64	122.67 ± 22.28	123.1473 ± 21.44	0.82
Daily energy intake (kcal)	2670.32 ± 750.17	2985.86 ± 693.26	2564.09 ± 739.32	<0.0001
History of HTN (%)	79.1	64.6	84.0	<0.0001
alcohol consumption (%)	0.9	3.5	0.0	<0.0001
Active smoking (%)	18.6	50.4	8.1	<0.0001
FBS	102.9 ± 41.44	101.91 ± 37.50	103.32 ± 42.73	
Cholesterol (mg/dl)	189.18 ± 43.27	176.13 ± 45.58	193.47 ± 41.59	<0.0001
TG (mg/dl)	142.13 ± 86.10	139.57 ± 97.57	143.11 ± 82.08	0.01
LDL (mg/dl)	108.86 ± 36.05	101.50 ± 37.52	111.22 ± 35.19	<0.0001
HDL (mg/dl)	81.85 ± 15.49	46.71 ± 14.29	53.57 ± 15.53	<0.0001
CVD mortality (%)	3.1	6.4	2.06	<0.0001
Values are presented as mean ± (standard deviation) or as % of patients.				
⊠Mann-Whitney U Tests, ⊠Chi-Square Tests				
BMI Body mass index, SBP Systolic blood pressure, DBP diastolic blood pressure, WHR waist to hip ratio, FBS Fast Blood Sugar, TG triglyceride, LDL Low-Density Lipoprotein, HDL High-Density Lipoprotein, CVD Cardiovascular Disease				

Dietary indices and intake of the participants of the study are presented in Table 2. As this Table indicates, the level of energy intake, macro- and micro-nutrients are significantly higher in men compared to women ($P = <0.05$). This Table did not show any significant difference in dietary indices among male and female participants of the study. (Table 2)

Table 2

Distribution of the level of energy intake, macro- and micro-nutrients, mean score of dietary indices and dietary acid load in men and women

	Total	Men (n=536)	Women (n=1622)	P value ^a
Daily energy intake [‡] (kcal)	3667.97 ± 16.16	2985.86 ± 693.26	2564.09 ± 739.32	<0.0001
Carbohydrate (gr)	465.01 ± 2.97	521.35 ± 5.61	446.40 ± 3.37	<0.0001
Protein (gr)	81.54 ± 0.55	91.81 ± 1.08	78.15 ± 0.62	<0.0001
Fat (gr)	58.04 ± 0.51	63.78 ± 1.10	56.14 ± 0.57	<0.0001
Monounsaturated fatty acid (gr)	16.98 ± 0.17	19.15 ± 0.41	16.26 ± 0.18	<0.0001
Polyunsaturated fatty acid (gr)	8.21 ± 0.08	9.12 ± 0.17	7.91 ± 0.09	<0.0001
Saturated fatty acid (gr)	22.09 ± 0.26	23.53 ± 0.55	21.62 ± 0.30	0.001
Alpha-Linolenic (gr)	0.33 ± 0.005	0.35 ± 0.011	0.32 ± 0.006	0.008
Linoleic (gr)	0.13 ± 0.002	0.35 ± 0.01	0.32 ± 0.006	0.008
Cholesterol (mg)	205.52 ± 2.50	250.47 ± 5.60	190.67 ± 2.67	<0.0001
DHA (gr)	0.03 ± 0.0005	0.04 ± 0.001	0.02 ± 0.0005	<0.0001
EPA (gr)	0.012 ± 0.0003	0.015 ± 0.0007	0.011 ± 0.0004	<0.0001
Sodium (mg)	1281.49 ± 4.13	1316.18 ± 2.12	1356 ± 2.42	<0.0001
Potassium (mg)	1157.35 ± 4.41	1212.12 ± 2.45	1102 ± 2.87	<0.0001
Fiber (gr)	27.06 ± 0.23	28.56 ± 0.46	26.56 ± 0.26	<0.0001
Calcium (mg)	513.88 ± 5.74	549.15 ± 10.89	502.22 ± 6.71	<0.0001
Vitamin D (IU)	36.24 ± 0.61	48.89 ± 1.43	32.05 ± 0.63	<0.0001
Vitamin C (mg)	141.47 ± 2.08	146.08 ± 3.78	139.95 ± 2.47	0.039
Vitamin E (mg)	36.24 ± 0.61	32.05 ± 0.63	12.56 ± 0.23	<0.0001
Vitamin K (Ug)	239.89 ± 5.91	235.13 ± 9.53	241.46 ± 7.21	0.510
Folate (mg)	374.92 ± 4.73	403.90 ± 9.48	365.35 ± 5.43	<0.0001
Iron (mg)	17.61 ± 0.12	19.26 ± 0.24	17.06 ± 0.14	<0.0001

EPA Eicosapentaenoic acid, DHA Docosahexaenoic acid, AHEI Alternative Healthy Eating Index, DII Dietary Inflammatory Index, NEAP Net Endogenous Acid Production

[‡]Mann-Whitney U Tests

	Total	Men (n=536)	Women (n=1622)	P value ^a
Zinc (mg)	6.40 ± 0.05	7.24 ± 0.11	6.12 ± 0.059	<0.0001
Magnesium (mg)	259.82 ± 2.26	288.42 ± 4.48	250.37 ± 2.57	<0.0001
Selenium (mg)	41.52 ± 0.47	49.89 ± 1.06	38.75 ± 0.49	<0.0001
AHEI score [‡]	62.05 ± 10.41	62.81 ± 10.96	61.79 ± 10.20	0.06
MDS score [‡]	9.12 ± 2.42	9.09 ± 2.45	9.14 ± 2.42	0.47
DASH score [‡]	3.45 ± 0.80	3.45 ± 0.82	3.44 ± 0.79	0.70
DII score [‡]	0.05 ± 2.62	-0.06 ± 2.44	0.08 ± 2.67	0.14
NEAP [‡]	49.42 ± 22.10	50.57 ± 24.88	49.00 ± 21.00	0.58
EPA Eicosapentaenoic acid, DHA Docosahexaenoic acid, AHEI Alternative Healthy Eating Index, DII Dietary Inflammatory Index, NEAP Net Endogenous Acid Production				
[‡] Mann-Whitney U Tests				

The association between different variables and CVDs mortality in a cox univariate model is shown in Table 3. It was revealed that being older (HR =1.065; 95% CI =1.02-1.1; P =0.001), having the history of HTN (HR =4.62; 95% CI =2.69-7.92; P =<0.0001), and being an active smoker (HR =1.78; 95% CI =1.02-3.11; P=0.041) were significantly associated with the increased risk of CVDs mortality. Also, there was an inverse significant relationship between the serum HDL- level and CVDs mortality (HR =0.97; 95% CI =0.95-0.99; P =0.02). (Table 3)

Table 3

The association between the variables and CVD mortality by cox regression analysis relationship in the whole

Variable	β	P_value	Hazard ratio (95% CI)
Age (year)	0.063	0.001	1.065 (1.02-1.1)
Weight (Kg)	0.030	0.129	1.030 (0.99-1.07)
BMI (kg/m ²)	-0.084	0.16	0.91 (0.81-1.034)
WHR	0.364	0.88	1.44 (0.01-1.97)
Physical activity(MET)	-0.027	0.17	0.12 (0.94-1.007)
DBP (mmHg)	-0.026	0.109	0.974(0.943-1.00)
SBP (mmHg)	0.008	0.409	1.008(0.98-1.02)
Daily energy intake (kcal)	0.00	0.24	1.00 (1.00-1.001)
History of HTN (%)	1.53	<0.0001	4.62 (2.69-7.92)
alcohol consumption (%)	0.28	0.78	1.32 (0.18-3.71)
Active smoking (%)	0.58	0.041	1.78 (1.02-3.11)
FBS	0.007	<0.0001	1.00 (1.00-1.01)
Cholesterol (mg/dl)	0.005	0.241	1.00 (0.99-1.01)
TG (mg/dl)	0.009	0.95	1.00 (0.75-1.35)
LDL (mg/dl)	0.04	0.95	1.04 (0.23-4.59)
HDL (mg/dl)	-0.02	0.02	0.97 (0.95-0.99)
BMI Body mass index, SBP Systolic blood pressure, DBP diastolic blood pressure, WHR waist to hip ratio, FBS Fast Blood Sugar, TG triglyceride, LDL Low-Density Lipoprotein, HDL High-Density Lipoprotein			

Table 4 demonstrates the associations among baseline dietary acid load and different dietary indices scores (DII, AHEI, MDS, and DASH scores), and CVDs mortality. As shown in the Table, there was not any significant relationship between dietary indices and CVDs mortality in the main univariate cox regression models. The confidence interval included 1.00 for NEAP score. However, the fully adjusted model (model 4) reports that there was a significant positive relationship between the baseline DII score and dietary acid load (NEAP score) level with CVDs mortality. (HR =1.11; 95% CI =1.01-1.24; P =0.04 and HR =1.02; 95% CI =1.01-1.03; P =<0.0001, respectively). We did not find any correlation between AHEI, MDS scores and CVD mortality. (Table 4)

Table 4

The association between diet quality indices, dietary acid load and CVD mortality by cox regression analysis relationship in the whole

	β	P-value	Hazard ratio (95% CI)
Model 1			
AHEI score	0.00	0.80	1.03 (0.97-1.02)
MED score	0.04	0.42	1.04 (0.93-1.16)
DASH score	0.24	0.12	0.78 (0.57-1.07)
DII score	0.07	0.15	1.07 (0.97-1.19)
NEAP	0.01	<0.0001	1.01 (1.00-1.02)
Model 2			
AHEI score	0.006	0.667	1.00 (0.98-1.03)
MED score	0.054	0.313	1.05 (0.95-1.17)
DASH score	-0.233	0.15	0.79 (0.57-1.08)
DII score	0.08	0.122	1.083 (0.97-1.19)
NEAP	0.01	0.001	1.01 (1.00-1.01)
Model 3			
AHEI score	0.008	0.527	1.00 (0.98-1.03)
MED score	0.046	0.396	1.04 (0.94-1.16)
DASH score	-0.274	0.09	0.76 (0.55-1.04)
DII score	0.115	0.035	1.12 (1.00-1.24)
NEAP	0.013	<0.0001	1.01 (1.00-1.02)
Model 4			
AHEI score	0.006	0.65	1.00 (0.98-1.03)
MED score	0.07	0.19	1.07 (0.96-1.20)
DASH score	-0.22	0.16	0.79 (0.57-1.09)
DII score	0.12	0.047	1.11 (1.01-1.24)
NEAP	0.02	<0.0001	1.02 (1.01-1.03)
AHEI Alternative Healthy Eating Index, DII Dietary Inflammatory Index, NEAP Net Endogenous Acid Production			

β	P-value	Hazard ratio (95% CI)
Model 1: No Adjusted		
Model 2: Adjusted for age, gender, smoking, alcohol intake, level of physical activity, family history of CVD and history of HTN		
Model 3: Adjusted for total energy, waist to hip ratio (WHR), BMI, weight, DBP, SBP, TG, Cholesterol, LDL and HDL		
Model 4: Adjusted for age, gender, smoking, alcohol intake, level of physical activity, family history of CVD, history of HTN, total energy, waist to hip ratio (WHR), BMI, weight, DBP, SBP, TG, Cholesterol, LDL and HDL		

Discussion

This retrospective cohort study was conducted to investigate the association between dietary indices and dietary acid load with CVD mortality in cardiovascular patients of Fasa Persian cohort. The results of this study showed that the CVD mortality rate increased significantly with age and simultaneous onset of hypertension; there was also a significant positive relationship between tobacco use and mortality from cardiovascular diseases. However, it was found that with increasing serum HDL levels, the mortality rate of CVD decreased significantly. In addition, there was a direct and significant association between DII score and dietary acid load with CVD mortality; thus, with an increase in DII score and dietary acid load, the rate of CVD mortality increased by 11% and 2%, respectively, while there was no significant correlation between AHEI and MDS scores with CVD mortality. The current study also revealed that adherence to the DASH diet in cardiovascular patients can reduce the risk of CVD mortality by 20.4%, but this decrease was not statistically significant although it is clinically significant.

In line with our study, *Jibin et Al.* (17) linked tobacco use and hypertension levels to mortality due to heart disease, stroke, and IHD. Nicotine and carbon monoxide available in tobacco promote the development of atherosclerosis by affecting myocardial oxygen capacity and increasing endothelial damage. Previous studies have also shown that tobacco use is closely linked to high hypertension and stroke. In addition, one of the main risk factors for heart disease is hypertension, and the severity of this disease can be controlled by reducing it.(17, 18)

This study also showed an inverse relationship between serum HDL levels and CVD mortality rate in patients. In this regard, *Chantal et al.* (19) reported high levels of serum HDL as a protective factor against mortality and cardiovascular diseases in people with diabetes. HDL plays a protective role against cardiovascular diseases and their mortality by clearing cholesterol from the macrophages and increasing endothelial function and antioxidant activities.(19)

Similar to our study, *Hoge et al.* (8) and *Shivappa et al.* (9) observed a direct association between CVD mortality and DII score. To explain this association, we can point to the relationship between high DII scores and increased risk of obesity, metabolic syndrome, and insulin resistance. (9, 20–22) These

chronic diseases are associated with inflammatory conditions in the body. Inflammatory biomarkers including hs-CRP, IL-6, IL-1B, TNF- α , IL-4, and IL-10 have also been shown to be connected with obesity, diabetes, and CVD. In this regard, previous studies have linked increased DII scores to high levels of cytokines such as IL-1, TNF- α , and CRP. On the other hand, the guidelines of AHA published in 2019 have introduced obesity and diabetes as two risk factors related with CVD mortality.(9, 23, 24)

According to the AHA-2019 guideline, energy, saturated and trans-fatty acids, cholesterol, red meat, and refined grains in the diet not only increase the DII score, but are also linked to increased mortality due to CVDs.(24) In contrast, the anti-inflammatory compounds such as vitamins C, E, beta-carotene, and zinc are associated with a decrease in DII score, and the antioxidant role of these compounds is a factor in the primary and secondary prevention of cardiovascular diseases. (8) In this regard, omega-3 fatty acids and polyphenols (found in vegetables and fruits) are associated with a decrease in DII score and inflammation rate in the body. They are involved in regulating the body's inflammatory processes, improving lipid profile, oxidative stress and endothelial function, and in this way, decreased the risk of chronic disorders such as cardiovascular disease. As a result, if dietary intake leads to inflammatory conditions, it can increase the risk of platelet aggregation and plaque formation at the endothelial cell, predisposing a patient to vascular damage and occlusion and increasing the risk of mortality.(22)

The results of our study demonstrated that there was a significant positive association between dietary acid load and risk of CVD mortality, so that by increasing a score in dietary acid load, the rate of CVD mortality increased by 2%. In of the same line with the present study, *Shamima et Al.* (6) detected a strong relationship among PRAL, NEAP scores, and CVD mortality rates. *Minseon et al.* (25) also linked an increased dietary acid load and a higher risk of CVD and all-cause mortality. Previous researches have shown that an increase in consumption of meat and its products, eggs, cheese, refined grains and fish, and a decrease in consumption of fruits and vegetables lead to an increase in the dietary acid load and risk of chronic diseases, including hypertension, cardiovascular diseases and type 2 diabetes and their mortality due to these diseases.(6, 25) In contrast to the consumption of potassium bicarbonate, magnesium, fiber, vitamin C, calcium and phytochemicals, which exist abundantly in fruits and vegetables (as part of a healthy diet); are probably associated with reduced dietary acid load and a lower risk of cardiovascular diseases.(6, 7, 16) Partial examination shows that a rise in acid load of diet, which is associated with an increase in blood acid levels, leads to the excretion of sodium in the body and an increase in cortisol secretion and insulin resistance. In this regard, the serum level of potassium reduces due to increased potassium excretion, which leads to an increase in hypertension by affecting vasodilation.(26) On the other hand, increased cortisol levels are related with metabolic syndrome and increased cardiovascular diseases and mortality risk.(27, 28) Insulin resistance is also caused by a reduced tendency for insulin to bind to its receptor in an acidic environment, which is directly related to the risk of CVD and all-cause mortality. (29, 30)

Phillips et al. (31) and *Fung et al.* (32) showed when the adherence to the DASH diet increases, the risk of cardiovascular diseases and mortality decreases. This decrease is due to the consumption of more vegetables, fruits, nuts and seeds, whole grains and low-fat dairy products and restrictions on the

consumption of red meat, sugars, sweets, beverages, and total and saturated fat. The mechanism of impact of this diet can be attributed to its compounds such as potassium, sodium, magnesium, calcium, fiber, and antioxidants. In this diet, high fiber intake leads to reduction in the levels of LDL, cholesterol, triglycerides, hypertension, CRP, and the risk of obesity and overweight, and improves insulin sensitivity and endothelial function.(4) DASH diet with emphasis on magnesium and potassium sources such as dark green leafy vegetables, seeds, nuts, and whole grains can play a role in controlling hypertension and stroke. Magnesium and potassium reduce inflammatory cytokines and increase nitric oxide levels, thereby affecting the severity of heart diseases and mortality due to them.(33, 34) According to our results, it was observed that adherence to the DASH diet in cardiovascular patients could reduce the risk of CVD mortality by 20.4%; however, this decrease was not statistically significant. In the same line with our study, *Ant Aigren et al.* \ did not found a strong relationship among DASH score and mortality from stroke.(3)

In the present study, we did not find a significant correlation between AHEI score and CVD related deaths. Contrary to our study, *Emily et al.* (35) reported that higher AHEI score led to lower risk of cardiovascular diseases and mortality by 16% and 34%, respectively. The AHEI score can assess the quality of the diet and predict the risk of death due to chronic diseases. The index measures consumption of whole grains, fruits, vegetables, fish, dairy, processed red meat, and alcohol. Also, *Akbaraly TN et al.* (5) in their study found that higher AHEI score had a significant inverse relationship with CVD mortality, while similar to the current study, no significant association was observed between this score and cancer related mortality. The most important reason for the inconsistency of the results of our study with other studies can be the short follow-up time.

In their study during 4 years, *Emily et al.* (4) recorded 1385 mortality cases from HF. In their study, similar to ours, there was no statistically significant relationship between MDS score and mortality. While *Hodge et al.* found that the more the adherence to the Mediterranean diet, the lower the risk of mortality at a young age. The Mediterranean diet improves systolic hypertension and lowers CRP, fibrinogen, oxidative stress and serum cholesterol, thereby reducing the incidence of chronic disorders and their mortality.(8, 34)

One of the main weaknesses of this study was the short follow-up time. Also, in this study, recall diet was not examined for nutritional assessment and only FFQ was used. Another weakness of this study was the recording of nutritional data in the baseline state and no other dietary record was recorded during the follow-up period; as a result, we were unable to assess the patients' dietary changes. Using self-reporting for food evaluation can also increase overestimation and underestimation. In this study, we failed to assess important factors such as disease severity, type of treatment during illness, and evaluation of health care that are associated with mortality. One of the strengths of this study is the study of dietary indices instead of evaluating specific micronutrients in the controls and inhibit of cardiovascular disease and its mortality. Also, in this study, four important indices were examined simultaneously, and this is of great importance. To summarize and comment definitively in this regard, it is suggested that studies with more follow-up years and the use of cohort studies should be carried out in other regions simultaneously.

Conclusion

The current study showed that increasing dietary acid load and the use of inflammatory food compounds increase the risk of CVD mortality. Adherence to the DASH diet can also be associated with reduced risk of mortality due to cardiovascular diseases in patients. Therefore, paying attention to the dietary acid load and acid balance along with the use of diets with anti-inflammatory properties and focusing on the DASH diet in CVD patients may be effective in preventing CVD mortality. However, more studies are needed in this regard.

Declarations

Ethical Approval and Consent to participate:

The present study was approved by the local Ethics Committee of Shiraz University of Medical Sciences, Shiraz, Iran (IR.SUMS.REC.1399.1116). The individuals who participated in the Persian cohort study signed the written consent forms.

Consent for publication:

All participants in Persian cohort study signed the approved informed consent to allow publication of anonymous data.

Availability of data and materials:

The data of this trial are available and can be obtained by sending email to the corresponding author, N.H (najmehhejazi@gmail.com)

Competing interests:

All the authors state that they have no conflict of interest.

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Authors' contributions:

S. Fereidooni: Conceptualization, Data collection, Data analysis, Manuscript writing

N. Hejazi: Conceptualization, Methodology, Project development, Data analysis, Manuscript writing, editing and approval.

R. Homayounfar: Project management, Investigation, methodology, Validation, review and editing of the manuscript.

M. Farjam: Project management, Investigation, Validation, review and editing of the manuscript.

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