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Association between alternate Mediterranean diet (aMED) and metabolic syndrome in Iranian elderly

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Background: Some food patterns and lifestyles have beneficial effects on diminution of Metabolic Syndrome (MetS) components. Alternate Mediterranean Diet (aMED) because of its contents may have potential protective impacts against the risk of developing the metabolic syndrome in elderly people. Our aim was to assess the association between aMED and MetS components in Iranian elderly.
Methods: 226 healthy elderly people (65 men and 161 women) with a mean age of 67.04 years participated in this cross-sectional study in five districts of Tehran, the capital of Iran during the period 20014-20015. MetS was defined based on the National Cholesterol Education Program Adult Treatment Panel III criteria. Dietary intakes were assessed using a validated food frequency questionnaire (FFQ) that included 147 items. The Alternate Mediterranean dietary score was calculated by Fung et al. Method. Logistic and linear regression models were used to derive beta estimates and odds ratios (ORs).
Results: Subjects in the top tertile of aMED had 56% lower chance of MetS compared with subjects in the bottom tertile (OR 0·46; 95% CI 0·23, 0·94; P trend=0.033). After adjustment for potential confounders such as age, energy intake, physical activity, marital status, smoking, education, income this association was strengthened (OR 0·34; 95% CI 0·14, 0·82; P trend=0.017). Also, it was observed that people in the highest tertile of the aMED score had 68% lower odds of high triglycerides compared with those in the lowest tertile (OR 0·42; 95% CI 0·20, 0·91; P trend=0.033).
Conclusion: Our study showed a higher adherence to the aMED reduced the risk of the MetS in the elderly subjects.

Introduction

Metabolic syndrome (MetS) (abdominal obesity, dyslipidemia, hypertension and hyperglycemia) is one of the major public health challenges in the worldwide, increasing the risk of cardiovascular disease and type 2 diabetes [1-3]. A recent estimation showed that 24% of the adult population in the United States were affected by MetS [4]. Similarly, metabolic syndrome with an estimated of 60%, is highly prevalent in Tehranian elderly [5]. Metabolic syndrome is determined by a variety of metabolic alteration with no single mechanism of etiology. There is a complex interaction between genetic, metabolic and environmental

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factors, including diet (especially unhealthy food patterns), lifestyles (such as overeating and sedentary lifestyle) and body fat accumulation are associated with this condition [6-10].

The National American Heart Association and Cholesterol Education Program Adult Treatment Panel III (NCEPATP III) have recommended diet-based plans as one principal method to prevent metabolic disorders and cardiovascular diseases[11, 12]. In the other words, adherence to healthy dietary patterns, for example, rich in fruit and vegetables and low in red meat, can prevent components of the MetS [13]. Among the commondietary patterns, Mediterranean diet demonstrated several health protective effects against the MetS [14]. But these reported mostly univocal results, were conducted on Mediterranean populations [15-20].

The investigators in Europe have extensively studied the alternate Mediterranean diet (aMED) as one of the other variations of the Mediterranean diet score (MDS). Alternate Mediterranean diet is different in the overall scales and in their measurement of individual dietary components such as alternatively, the ratio of MUFA: SFA and assessment of olive oil intake as separate items. aMED has scores ranging from 0 to 9 and was created by the association of the risk of chronic disease in North American populations [21]. Studies illustrated that both of the Mediterranean diet and aMED consistently linked with reducing the risks of CVD [22-25]. Therefore, aMED might be associated with metabolic syndrome as one of the risk factors of heart diseases. So the aim of this study is an exploration of the association between aMED and components of metabolic syndrome in Iranian elderly.

Material and methods

Study population

The study was a representative cross-sectional survey targeting resident elderly in five districts of Tehran, the capital of Iran. Here, 226 healthy elderly people (65 men and 161 women) with a mean age of 67.04 (60-83) years during the period 2014-2015, were randomly selected through a two-stage random cluster sampling among elder people who attended the Tehran Health centers (Tehran, Iran). For this purpose, Tehran was divided into five regions: North, South, East, West and Central districts then a list of health centers in each area was prepared and 25 of them were selected randomly (in attention to constraints budget and time). Then the total number of samples (226) divided by the number of health centers [25] and obtained the number of samples in each home centers. Inclusion criteria were age over 60 years, would like to participate in the study, ability to answer questions, no clinical symptoms of cardiovascular, renal, gastrointestinal disease and other endocrine and thyroid disease.

Assessment of dietary intake

Usual dietary intakes over the one past year were assessed by trained experts using food frequency questionnaire (FFQ) containing 147 food items. Previous studies have proven the reliability and validation of the questionnaire [26-28]. The interviewer filled FFQ for each individual depending on his or her intake per day, week, month, and year. Then the reported amounts were converted to grams per day. The Nutritionist IV computer software was used to the analysis of macronutrients and micronutrients in diet for each person.

Adherence to Alternate Mediterranean dietary pattern

The alternate Mediterranean dietary score was calculated by Fung et al method [29], based on nine foods component and nutrients includes: total vegetables except for potatoes, nuts, legumes, fish, all fruit, whole grains, MUFA to SFA ratio, alcohol and red and processed meat. Intakes total vegetables except potatoes, nuts, legumes, fish, all fruit, whole grains, MUFA to SFA ratio above the median of the study population received 1 point and intakes under the median of the study subjects received 0 point whereas intakes red and processed meat under the median of the study population received 1 point and intakes above the median of the study subjects received 0 point. Alcohol was not considered in our calculations because none of our participants consumed alcohol. Finally, the scores were collected and the individuals were categorized based on the tertiles of Alternate Mediterranean diet scores.

Anthropometric measurements

Table 1. General Characteristics of the participants based on tertiles of aMed Diet Index

		Alternate Mediterranean Diet Score tertiles**			P Value*
		1 (n=134)	2 (n=34)	3 (n=58)	
Age(years)		65.94±5.82	67.86±5.77	65.81±5.40	0.037
Sex (M/F) (%)	Male	30.6%	20.6%	29.3%	0.512
	Female	69.4%	79.4%	70.7%	
Weight(kg)		71.50±11.83	73.05±10.01	74.94±13.38	0.188
WC(cm)		98.38±10.97	100.27±8.38	100.5679±9.97	0.333
BMI(kg/m^2)		29.38±4.78	30.14±3.85	30.38±4.30	0.323
Obese	BMI≥30	62.7%	50%	44.8%	0.053
Marital status	Single	1.5%	0.0%	1.7%	0.659
	Married	71.6%	61.8%	75.9%	
	Divorced	2.2%	29%	0.0%	
	Widow	24.6%	35.3%	22.4%	
Income	Low	56.8%	52.9%	43.9%	0.523
	Medium	35.6%	41.2%	49.1%	
	High	7.6%	5.9%	7.0%	
Smoking	None smoker	88.8%	76.5%	79.3%	0.276
	Former smoker	8.2%	14.7%	13.8%	
	Current smoker	3.0%	8.8%	6.9%	
Physical activity	Low	87.3%	88.2%	67.2%	0.002
	Moderate	12.7%	11.8%	32.8%	

BMI, Body Mass Index; WC, Waist circumference

* Obtained from ANOVA for continuous variables and $\chi 2$ test for categorical variables

Was measured height without shoes by a wall stadiometer (stadiometer) with a sensitivity 0.1 cm (Seca, Germany) and weight by digital scale (808 Seca, Germany) with an accuracy 0.1 kg with light clothes (without a coat and rain coat). BMI was calculated by dividing weight in kilograms by the square of height in meters. Waist circumference was measured with a tape measure between the iliac crest and the lowest rib on the exhale.

Assessment of blood pressure

Blood pressure was measured by a digital manometer (BC 08, Beurer, Germany) after at least 10-15 minutes of resting. Blood pressure was measured twice for each person and then the average values, were reported.

Biochemical assessments

10 ml of blood samples were taken between the hours of 7-10 am from all of fasted participants and were collected in acid-washed tubes test without anticoagulant. After storing at room temperature for 30 minutes and clot formation, blood samples were centrifuged at 1500 g for 20 minutes. Serums were stored in -80° C until future testing. Measurement of serum glucose, triglyceride and HDL-C was performed by an enzymatic method, using commercial kits (Pars test, Iran) and automated device (Selecta E, Vitalab, Netherland).

Assessment of metabolic syndrome

Metabolic syndrome was defined according to the definition of the National Cholesterol Education Program- Adult Treatment Panel III criteria (NCEP-ATP III) in the presence of three of the five risk factors include: abdominal obesity(waist circumferences ≥102 cm for men and ≥88 cm for women), hypertension(SBP ≥130 mmHg or DBP ≥ 85 mmHg), hyper-triglyceridemia(serum triglyceride level ≥150 mg/dl), low HDL-C (HDL-C ≤50 mg/dl and ≤40 mg/dl for women and men, respectively), hyperglycemia(FBS ≥ 100 mg/dl).

Statistical methods

People were categorized based on the tertiles of the Alternate Mediterranean diet score. For comparison general characteristics among the tertiles of Alternate Mediterranean diet scores, one-way ANOVA and Chi-square tests were used respectively for quantitative and qualitative variables. ANCOVA was used for multivariable-adjusted intakes foods and Energy of study participants across tertiles of Alternate Mediterranean Diet Index.We performed multiple linear and logistic regression to calculate adjusted beta estimates and odds ratios to assess the association between Alternate

Table 2. Multivariable-adjusted intakes foods and energy for the participants across tertiles of aMED Index

	Mean consumption in all (226)	Tertiles of aMED Index			P-value*
		1 (n=134)	2 (n=34)	3 (n=58)	
Energy(kcal/day)	2775.69±799.09	2581.68±736.30	2824.91±724.47	2923.06±896.69	0.025
Nutrients					
Carbohydrates (g/d)	371.23±137.21	324.29±102.99	380.48±75.62	474.23±173.88	<0.0001
Proteins (g/d)	84.15±31.74	74.82±25.49	82.34±20.24	106.75±38.69	<0.0001
Fats(g/d)	78.95±36.48	67.74±22.79	89.40±55.46	98.72±38.76	<0.0001
Dietary fibre (g/d)	46.77±24.70	40.58±19.53	46.09±18.19	61.45±31.89	0.004
n-3 Fatty acids (g/d)	1.23±0.87	1.07±0.92	1.39±0.89	1.50±0.66	0.076
Calcium(mg/d)	1138.75±433.35	1054.99±373.81	1036.31±333.51	1392.31±512.49	0.071
Food groups					
Vegetable(g/d)	422.73±220.12	347.71±158.28	442.95±216.27	584.21±256.36	<0.0001
Fruit(g/d)	426.36±255.93	351.75±196.57	406.61±197.68	610.28±313.12	<0.0001
Legumes and Nuts (g/d)	48.46±38.92	35.05±23.72	57.17±42.78	74.35±49.55	<0.0001
Whole grains(g/d)	48.46±38.92	33.45±22.37	48.26±35.89	63.87±48.35	<0.0001
Red and processed meats(g/d)	22.90±25.06	29.12±36.05	20.26±15.46	19.23±17.11	0.649
Fish(g/d)	0.6±1.58	0.4±0.94	0.5±1.17	0.7±2.30	0.649
Low-fat dairy products (g/d)	292.68±223.42	289.20±218.26	237.71±197.68	332.96±244.49	0.209
High-fat dairy products (g/d)	91.81±124.76	82.39±108.99	91.44±121.98	113.80±156.26	0.949

* Obtained from ANCOVA and P-value is considered significant at p<0.05
¥Energy intake is adjusted for age and sex; all other values are adjusted for age, sex and energy intake.

Mediterranean diet score with metabolic syndrome in three models. All analyses were conducted by using a Statistical Package for the Social Sciences (SPSS) software, version 22 and for all the tests P-value less than 0.05was considered significant.

Results

General characteristics of 226 healthy elderly people are reported based on tertiles of the Alternate Mediterranean diet score in Table 1. Participants in the highest tertile of the Alternate Mediterranean diet score had likely more physical activity compared with individuals in the lowest tertile and age was statistically significant differences among tertiles of Alternate Mediterranean diet score. Statistically significant differences were not seen for the other variables.

Usual intakes of selected food and nutrient groups across on tertiles of the Alternate Mediterranean diet score are provided in Table 2. Individuals in the highest tertile of the Alternate Mediterranean diet score had significantly higher intakes of energy, carbohydrates, proteins, fats, dietary fiber, fruits, vegetables, nuts and legumes, whole grains. Whereas for the other food and nutrient groups were not observed a significant association.

Multivariable-adjusted OR and beta estimates for metabolic syndrome based on the tertile of Alternate Mediterranean diet score are presented in Table 3. In crude model, subjects in the top tertile of Alternate Mediterranean diet had 56% lower chance of metabolic syndrome compared with subjects in the bottom tertile (OR 0·44; 95% CI 0·23, 0·94) and a significant inverse

Table 3. Beta estimates and odds ratios of MetS based on the tertiles of aMED Index

Variables	MetS (Tertiles of aMED)			P trend	Beta estimates	SE	*p* value
	1(n=134)	2(n=34)	3(n=58)				
Crude model	1.00	0.74 (0.33-1.64)	0.46 (0.23-0.94)	0.033	-0.75	0.35	0.034
*Model 1	1.00	0.69 (0.31-1.54)	0.38 (0.17-0.83)	0.015	-0.95	0.39	0.016
**Model 2	1.00	0.72 (0.31-1.68)	0.34 (0.14-0.82)	0.017	-1.06	0.44	0.016

* Model 1: Adjusted for age and energy intake
**Model 2: Adjusted for age, energy intake, physical activity, marital status, smoking, education, income

Table 4. Odds ratios for MetS components based on the tertiles of aMED Score

	Tertiles of aMED			P trend
	1(n=134)	2(n=34)	3(n=58)	
Central obesity				
Model 1	1.00	0.63 (0.23-1.63)	0.38 (0.15-0.97)	0.038
Model 2	1.00	0.78 (0.18-3.33)	0.27 (0.07-1.01)	0.050
High triglycerides				
Model 1	1.00	0.65 (0.30-1.41)	0.48 (0.24-0.96)	0.033
Model 2	1.00	0.65 (0.28-1.46)	0.42 (0.20-0.91)	0.033
Hypertension				
Model 1	1.00	0.57 (0.22-1.47)	0.66 (0.30-1.46)	0.250
Model 2	1.00	0.59 (0.22-1.57)	0.70 (0.30-1.61)	0.302
Low HDL cholesterol				
Model 1	1.00	0.96 (0.43-2.13)	0.83 (0.41-1.65)	0.610
Model 2	1.00	0.99 (0.43-2.27)	0.72 (0.34-1.51)	0.416
High glucose				
Model 1	1.00	1.43 (0.63-3.22)	0.75 (0.37-1.52)	0.577
Model 2	1.00	1.29 (0.55-3.05)	0.65 (0.30-1.40)	0.329

*Model 1: Age and energy intake
¥ Model 2: Model 1 additionally for sex, physical activity, education, marital status, smoking

association was observed between metabolic syndrome and Alternate Mediterranean diet score (β=−0.75; SE=0.35). After adjustment for potential confounders such as age, energy intake, physical activity, marital status, smoking, education, income this association was strengthened (OR 0·34, 95% CI 0·14, 0·82; β = −1.06, SE=0.44).

The odds of developing metabolic syndrome components are provided in Table 4. After controlling for potential confounders, it was observed that those in the highest tertile of the alternate Mediterranean diet score had 68% lower odds of high triglycerides compared with those in the lowest tertile (OR 0·42; 95% CI 0·20, 0·91). Also, we found that a high adherence to aMED, was slight significantly associated with the central obesity than the other groups (OR 0·27; 95% CI 0·07, 1·01).

Discussion

The present study showed that a higher adherence to the alternate Mediterranean diet reduced the risk of the metabolic syndrome in the elderly people. In this study the risk of hypertriglyceridemia as one of the metabolic syndrome components was lower in elderly people who had more adherence to this diet. Also, we found that a high adherence to aMED, was slight significantly associated with the central obesity than the other groups.

The aMED score was updated by Fung et al.[30] of the Mediterranean Diet Score [31]. Similar to our results several studies of the MED adherence have been inversely associated with waist circumference[32, 33]. Both traditional scores of the Mediterranean diet (MDS) and aMED because of having the larger amounts of whole grains and fibers were related to lower central adiposity[34, 35]. On the other hand, the aMED is a high-fat and high-unsaturated fat food pattern because it consisted of the foods such as nuts and olive oil. Nevertheless, in some studies, there was a weak positive association between the total fat intake and weight gain[36]. Some researchers demonstrated that the type of fat is more important than the amount consumed fats in adiposity progress[36, 37]. Among of the fatty acids, monounsaturated fatty acids (MUFA) and polyunsaturated fatty acids (PUFA) was not associated with weight gain in the Nurses' Health Study[36]. Furthermore the increase consumption of fruit and vegetable and decrease the unhealthy and fast food intake in the MED has been demonstrated to protect against weight gain and obesity [38, 39].

In the present study, the risk of hypertriglyceridemia was lower in the highest adherence to the aMED in elderly people. Studies recommended that a diet rich in PUFA (omega-3 fatty acid rich oils, cold water fish, walnuts) and MUFA, fiber, with limited carbohydrates that contribute to a high glycemic load, decrease triglycerides and increase serum HDL-cholesterol levels [40-44]. MED is a food pattern that rich in mention nutrients[45]. Also, several studies have shown that MED decreased the TG and increased the HDL cholesterol levels[46, 47].

Our finding about HDL cholesterol levels was not significant. Gerasimova et al., in the Alaskan population study concluded that the regular consumption of dietary omega-3 fatty acids, enhanced HDL cholesterol levels[48]. In our study, the differences in omega-3 fatty acids and fish intakes were not significant among the tertiles of the adherence to the aMED adherence. Generally, previous studies indicated the consumption of fish and marine sources of omega-3(as important factors to increase the HDL cholesterol levels) is low in Iranian population especially elderly people[49]. This matter also may be affected the serum glucose, because some studies demonstrated the beneficial effects of omega-3 fatty acids on the impaired glucose tolerance or the risk of diabetes[50, 51].While we not able find the statistically associated between aMED adherence and high glucose level. Moreover, in this present study the intakes of meat and process meat are high in the tertiles of aMED adherence. There are some evidences that showed meat and processed meat have undesirable effects on glucose metabolism[52, 53].

The MED has many of the characteristics of the DASH (Dietary Approaches to Stop Hypertension) diet,such as the great intakes of vegetables and fruits[54]. So far some articles have described an inverse association between MED adherence and blood pressure[54, 55]. In contrast to mention studies we have not documented the significant association between aMED adherence and blood pressure. The potassium and magnesium, which were found in abundance in fruits and vegetables can affect the blood pressure[56, 57], studies suggest that calcium is also largely implicated in regulating blood pressure[58]. Although the calcium intakes of elderly participants in our study increased with enhancement of adherence to the aMED, but the difference of calcium intakes among three groups was not significant. Also in this present study, the consumption of high fat dairy products in higher adherence to aMED was higher than other groups. The more consistent finding was observed in relation to the effect of low-fat dairy products on hypertension [53, 59]. Low-fat dairy products are established hypotensive properties because of rich in calcium, potassium and magnesium[60]. Despite this contradiction between the results of the metabolic syndrome components and aMED scores in our study, the association of the adherence to the aMED and the risk of metabolic syndrome is statistical. There is no evidence for the effects of aMED adherence and incidence of metabolic syndrome. Although the recent studies indicated that the aMED score has a strong association with disease and mortality. Jacobs et al. conducted the Multiethnic Cohort study in Hawaii and California to survey the association of four diet quality indexes with Colorectal cancer and all-cause mortality. This study demonstrated that only increased adherence to aMED among diet quality indexes decreased colorectal cancer and mortality in African-American women [61]. In another Multiethnic Cohort study performed by Shvetsov et al., a higher aMED score was associated with lower risk of CVD and cancer mortality [62]. Since the metabolic syndrome is a risk factor for cardiovascular disease and mortality[63] Somehow, the results of the mentioned investigations were in the same line of the present study that higher adherence to aMED was an associated with lower risk of metabolic syndrome in the elderly population. Chronic inflammation plays an important role in metabolic syndrome which among inflammatory markers hs-CRP, TNF-α, fibrinogen, and IL-6 are linked with waist circumference, fasting insulin, and HOMA-IR in MS subjects [64, 65]. The inverse association between aMED and metabolic syndrome is likely to be mediated by the anti-inflammatory effect of this diet because aMED is an anti-inflammatory diet reducing concentrations of biomarkers of inflammation and endothelial dysfunction such as CRP, IL-6, E-selectin, sICAM-1[30, 66].

In summary, these findings indicate that the altered Mediterranean diet index which is characterised by high consumption of olive oil, fruits, vegetables, whole grains, legumes and other food components that are rich in nutrients, including monounsaturated fat, fibre, Ca, Mg, phytooestrogens, antioxidants[67] is beneficial for the reduction the risk of metabolic syndrome in elderly people.

Limitations

This is a cross-sectional study, so it could not establish causal relationships but only state hypotheses about the link between metabolic syndrome and alternate Mediterranean diet in elderly people. Therefore, the possible modest impact of the Mediterranean diet on metabolic syndrome components (lipid profile, weight, glucose level and blood pressure levels) in elderly people should be further investigated by randomized clinical trials. Another limitation of our study is concerning a possible overestimation or underestimation of dietary intakes, because the participants in the study were elderly and FFQ is a memory-based questionnaire. So that misreporting of food items consumed could influence the calculation of the diet score and bias the results of the data analysis.

Conclusion

To the best of our knowledge this is the first cross-sectional study that shows that this high adherence to the alternate Mediterranean dietary pattern can reduce the risk of metabolic syndrome in elderly people. However, some components of metabolic syndrome in this study not showed a significant relationship with higher adherence to the alternate Mediterranean diet. Therefore, further investigation is needed in this field.

Conflict of interest

There are no competing financial interests.

References

1. Eckel RH, Grundy SM, Zimmet PZ. The metabolic syndrome. The lancet. 2005;365(9468):1415-28.
2. Pacifico L, Anania C, Martino F, Poggiogalle E, Chiarelli F, Arca M, et al. Management of metabolic syndrome in children and adolescents. Nutrition, Metabolism and Cardiovascular Diseases. 2011;21(6):455-66.
3. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. Journal of the American College of Cardiology. 2007;49(4):403-14.
4. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey. Jama. 2002;287(3):356-9.
5. Azizi F, Salehi P, Etemadi A, Zahedi-Asl S. Prevalence of metabolic syndrome in an urban population: Tehran Lipid and Glucose Study. Diabetes research and clinical practice. 2003;61(1):29-37.
6. Anagnostis P. Metabolic syndrome in the Mediterranean region: Current status. Indian journal of endocrinology and metabolism. 2012;16(1):72.
7. Di Renzo L, Marsella LT, Sarlo F, Soldati L, Gratteri S, Abenavoli L, et al. C677T gene polymorphism of MTHFR and metabolic syndrome: response to dietary intervention. Journal of translational medicine. 2014;12(1):329.
8. Di Renzo L, Rizzo M, Iacopino L, Sarlo F, Domino E, Jacoangeli F, et al. Body composition phenotype: Italian Mediterranean Diet and C677T MTHFR gene polymorphism interaction. Eur Rev Med Pharmacol Sci. 2013;17(19):2555-65.
9. Groop L. Genetics of the metabolic syndrome. British Journal of Nutrition. 2000;83(S1):S39-S48.
10. Lidfeldt J, Nyberg P, Nerbrand C, Samsioe G, Scherstén B, Agardh C-D. Socio-demographic and psychosocial factors are associated with features of the metabolic syndrome. The Women's Health in the Lund Area (WHILA) study. Diabetes, Obesity and Metabolism. 2003;5(2):106-12.
11. Expert Panel on Detection E. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (Adult Treatment Panel III). Jama. 2001;285(19):2486.
12. Sonnenberg L, Pencina M, Kimokoti R, Quatromoni P, Nam BH, D'agostino R, et al. Dietary patterns and the metabolic syndrome in obese and non-obese Framingham women. Obesity. 2005;13(1):153-62.
13. Grosso G, Mistretta A, Frigiola A, Gruttadauria S, Biondi A, Basile F, et al. Mediterranean diet and cardiovascular risk factors: a systematic review. Critical reviews in food science and nutrition. 2014;54(5):593-610.
14. Grosso G, Buscemi S, Galvano F, Mistretta A, Marventano S, La Vela V, et al. Mediterranean diet and cancer: epidemiological evidence and mechanism of selected aspects. BMC surgery. 2013;13(2):S14.
15. Grosso G, Mistretta A, Marventano S, Purrello A, Vitaglione P, Calabrese G, et al. Beneficial effects of the Mediterranean diet on metabolic syndrome. Current pharmaceutical design. 2014;20(31):5039-44.
16. Grosso G, Marventano S, Galvano F, Pajak A, Mistretta A. Factors associated with metabolic syndrome in a Mediterranean population: role of caffeinated beverages. Journal of Epidemiology. 2014;24(4):327-33.
17. Bibiloni MM, Martínez E, Llull R, Maffiotte E, Riesco M, Llompart I, et al. Metabolic syndrome in adolescents in the Balearic Islands, a Mediterranean region. Nutrition, Metabolism and Cardiovascular Diseases. 2011;21(6):446-54.
18. Kesse-Guyot E, Ahluwalia N, Lassale C, Hercberg S, Fezeu L, Lairon D. Adherence to Mediterranean diet reduces the risk of metabolic syndrome: a 6-year prospective study. Nutrition, Metabolism and Cardiovascular Diseases. 2013;23(7):677-83.
19. di Giuseppe R, Bonanni A, Olivieri M, Di Castelnuovo A, Donati MB, de Gaetano G, et al. Adherence to Mediterranean diet and anthropometric and metabolic parameters in an observational study in the ‘Alto Molise’region: the MOLI-SAL project. Nutrition, Metabolism

and Cardiovascular Diseases. 2008;18(6):415-21.
20. Bach-Faig A, Berry EM, Lairon D, Reguant J, Trichopoulou A, Dernini S, et al. Mediterranean diet pyramid today. Science and cultural updates. Public health nutrition. 2011;14(12A):2274-84.
21. Shvetsov YB, Harmon BE, Ettienne R, Wilkens LR, Le Marchand L, Kolonel LN, et al. The influence of energy standardisation on the alternate Mediterranean diet score and its association with mortality in the Multiethnic Cohort. British Journal of Nutrition. 2016;116(9):1592-601.
22. Trichopoulou A, Martínez-González MA, Tong TY, Forouhi NG, Khandelwal S, Prabhakaran D, et al. Definitions and potential health benefits of the Mediterranean diet: views from experts around the world. BMC medicine. 2014;12(1):112.
23. Sofi F, Macchi C, Abbate R, Gensini GF, Casini A. Mediterranean diet and health status: an updated meta-analysis and a proposal for a literature-based adherence score. Public health nutrition. 2014;17(12):2769-82.
24. Fung TT, Rexrode KM, Mantzoros CS, Manson JE, Willett WC, Hu FB. Mediterranean diet and incidence of and mortality from coronary heart disease and stroke in women. Circulation. 2009;119(8):1093-100.
25. De Koning L, Chiuve SE, Fung TT, Willett WC, Rimm EB, Hu FB. Diet-quality scores and the risk of type 2 diabetes in men. Diabetes care. 2011;34(5):1150-6.
26. Asghari G, Rezazadeh A, Hosseini-Esfahani F, Mehrabi Y, Mirmiran P, Azizi F. Reliability, comparative validity and stability of dietary patterns derived from an FFQ in the Tehran Lipid and Glucose Study. British journal of nutrition. 2012;108(06):1109-17.
27. Mirmiran P, Esfahani FH, Mehrabi Y, Hedayati M, Azizi F. Reliability and relative validity of an FFQ for nutrients in the Tehran Lipid and Glucose Study. Public health nutrition. 2010;13(05):654-62.
28. Hosseini Esfahani F, Asghari G, Mirmiran P, Azizi F. Reproducibility and relative validity of food group intake in a food frequency questionnaire developed for the Tehran Lipid and Glucose Study. Journal of epidemiology. 2010;20(2):150-8.
29. Fung TT, McCullough ML, Newby P, Manson JE, Meigs JB, Rifai N, et al. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. The American journal of clinical nutrition. 2005;82(1):163-73.
30. Fung TT, McCullough ML, Newby PK, Manson JE, Meigs JB, Rifai N, et al. Diet-quality scores and plasma concentrations of markers of inflammation and endothelial dysfunction. The American journal of clinical nutrition. 2005;82(1):163-73.
31. Trichopoulou A, Costacou T, Bamia C, Trichopoulos D. Adherence to a Mediterranean diet and survival in a Greek population. New England Journal of Medicine. 2003;348(26):2599-608.
32. Liese AD, Schulz M, Moore CG, Mayer-Davis EJ. Dietary patterns, insulin sensitivity and adiposity in the multi-ethnic Insulin Resistance Atherosclerosis Study population. British journal of nutrition. 2004;92(06):973-84.
33. Wirfält E, Hedblad B, Gullberg B, Mattisson I, Andrén C, Rosander U, et al. Food patterns and components of the metabolic syndrome in men and women: a cross-sectional study within the Malmö Diet and Cancer cohort. American Journal of Epidemiology. 2001;154(12):1150-9.
34. Koh-Banerjee P, Franz M, Sampson L, Liu S, Jacobs DR, Spiegelman D, et al. Changes in whole-grain, bran, and cereal fiber consumption in relation to 8-y weight gain among men. The American journal of clinical nutrition. 2004;80(5):1237-45.
35. Liu S, Willett WC, Manson JE, Hu FB, Rosner B, Colditz G. Relation between changes in intakes of dietary fiber and grain products and changes in weight and development of obesity among middle-aged women. The American journal of clinical nutrition. 2003;78(5):920-7.
36. Field AE, Willett WC, Lissner L, Colditz GA. Dietary fat and weight gain among women in the Nurses' Health Study. Obesity. 2007;15(4):967-76.
37. Koh-Banerjee P, Chu N-F, Spiegelman D, Rosner B, Colditz G, Willett W, et al. Prospective study of the association of changes in dietary intake, physical activity, alcohol consumption, and smoking with 9-y gain in waist circumference among 16 587 US men. The American journal of clinical nutrition. 2003;78(4):719-27.
38. Vioque J, Weinbrenner T, Castelló A, Asensio L, Hera MG. Intake of fruits and vegetables in relation to 10-year weight gain among Spanish adults. Obesity. 2008;16(3):664-70.
39. He K, Hu F, Colditz G, Manson J, Willett W, Liu S. Changes in intake of fruits and vegetables in relation to risk of obesity and weight gain among middle-aged women. International journal of obesity. 2004;28(12):1569-74.
40. Nordmann AJ, Nordmann A, Briel M, Keller U, Yancy WS, Brehm BJ, et al. Effects of low-carbohydrate vs low-fat diets on weight loss and cardiovascular risk factors: a meta-analysis of randomized controlled trials. Archives of internal medicine. 2006;166(3):285-93.
41. Frost G, Leeds A, Dore C, Madeiros S, Brading S, Dornhorst A. Glycaemic index as a determinant of serum HDL-cholesterol concentration. The Lancet. 1999;353(9158):1045-8.
42. Katan MB. Effect of low-fat diets on plasma high-density lipoprotein concentrations. The American journal of clinical nutrition. 1998;67(3):573S-6S.

43. Kris-Etherton PM, Harris WS, Appel LJ. Fish consumption, fish oil, omega-3 fatty acids, and cardiovascular disease. circulation. 2002;106(21):2747-57.
44. Lecumberri E, Goya L, Mateos R, Alía M, Ramos S, Izquierdo-Pulido M, et al. A diet rich in dietary fiber from cocoa improves lipid profile and reduces malondialdehyde in hypercholesterolemic rats. Nutrition. 2007;23(4):332-41.
45. Knoops KT, de Groot LC, Kromhout D, Perrin A-E, Moreiras-Varela O, Menotti A, et al. Mediterranean diet, lifestyle factors, and 10-year mortality in elderly European men and women: the HALE project. Jama. 2004;292(12):1433-9.
46. Chrysohoou C, Panagiotakos DB, Pitsavos C, Das UN, Stefanadis C. Adherence to the Mediterranean diet attenuates inflammation and coagulation process in healthy adults: The ATTICA Study. Journal of the American College of Cardiology. 2004;44(1):152-8.
47. Tzima N, Pitsavos C, Panagiotakos DB, Skoumas J, Zampelas A, Chrysohoou C, et al. Mediterranean diet and insulin sensitivity, lipid profile and blood pressure levels, in overweight and obese people; the Attica study. Lipids in Health and Disease. 2007;6(1):22.
48. Gerasimova E, Perova N, Ozerova I, Polessky V, Metelskaya V, Sherbakova I, et al. The effect of dietary n− 3 polyunsaturated fatty acids on HDL cholesterol in Chukot residentsvs muscovites. Lipids. 1991;26(4):261-5.
49. Hamideh S, Behzad M, Ebrahim G, Hassan E, Mojtaba S. Diet, hypertension, hypercholesterolemia and diabetes in ischemic heart diseases. Pakistan Journal of Medical Sciences. 2007;23(4):597.
50. Feskens EJ, Bowles CH, Kromhout D. Inverse association between fish intake and risk of glucose intolerance in normoglycemic elderly men and women. Diabetes care. 1991;14(11):935-41.
51. Djoussé L, Gaziano JM, Buring JE, Lee I-M. Dietary omega-3 fatty acids and fish consumption and risk of type 2 diabetes. The American journal of clinical nutrition. 2011;93(1):143-50.
52. Van Dam RM, Willett WC, Rimm EB, Stampfer MJ, Hu FB. Dietary fat and meat intake in relation to risk of type 2 diabetes in men. Diabetes care. 2002;25(3):417-24.
53. Pereira MA, Jacobs Jr DR, Van Horn L, Slattery ML, Kartashov AI, Ludwig DS. Dairy consumption, obesity, and the insulin resistance syndrome in young adults: the CARDIA Study. Jama. 2002;287(16):2081-9.
54. Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A. Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) study. The American journal of clinical nutrition. 2004;80(4):1012-8.
55. León EEÁ, Barba LR, Majem LS. Prevalencia del síndrome metabólico en la población de la Comunidad Canaria. Medicina clínica. 2003;120(5):172-4.
56. Geleijnse J, Kok F, Grobbee D. Blood pressure response to changes in sodium and potassium intake: a metaregression analysis of randomised trials. Journal of human hypertension. 2003;17(7):471-80.
57. Mizushima S, Cappuccio F, Nichols R, Elliott P. Dietary magnesium intake and blood pressure: a qualitative overview of the observational studies. Journal of human hypertension. 1998;12(7):447-53.
58. Allender PS, Cutler JA, Follmann D, Cappuccio FP, Pryer J, Elliott P. Dietary Calcium and Blood PressureA Meta-Analysis of Randomized Clinical Trials. Annals of internal medicine. 1996;124(9):825-31.
59. Toledo E, Delgado-Rodríguez M, Estruch R, Salas-Salvadó J, Corella D, Gomez-Gracia E, et al. Low-fat dairy products and blood pressure: follow-up of 2290 older persons at high cardiovascular risk participating in the PREDIMED study. British Journal of Nutrition. 2009;101(01):59-67.
60. Meisel H. Biochemical properties of peptides encrypted in bovine milk proteins. Current medicinal chemistry. 2005;12(16):1905-19.
61. Jacobs S, Harmon BE, Ollberding NJ, Wilkens LR, Monroe KR, Kolonel LN, et al. Among 4 Diet Quality Indexes, Only the Alternate Mediterranean Diet Score Is Associated with Better Colorectal Cancer Survival and Only in African American Women in the Multiethnic Cohort. The Journal of nutrition. 2016;146(9):1746-55.
62. Shvetsov YB, Harmon BE, Ettienne R, Wilkens LR, Le Marchand L, Kolonel LN, et al. The influence of energy standardisation on the alternate Mediterranean diet score and its association with mortality in the Multiethnic Cohort. The British journal of nutrition. 2016;116(9):1592-601.
63. Lakka HM, Laaksonen DE, Lakka TA, Niskanen LK, Kumpusalo E, Tuomilehto J, et al. The metabolic syndrome and total and cardiovascular disease mortality in middle-aged men. Jama. 2002;288(21):2709-16.
64. Farooq W, Farwa U, Khan FR. The metabolic syndrome and inflammation: role of insulin resistance and increased adiposity. Oman medical journal. 2015;30(2):100-3.
65. Sutherland JP, McKinley B, Eckel RH. The metabolic syndrome and inflammation. Metabolic syndrome and related disorders. 2004;2(2):82-104.
66. Park KH, Zaichenko L, Peter P, Davis CR, Crowell JA, Mantzoros CS. Diet quality is

associated with circulating C-reactive protein but not irisin levels in humans. Metabolism: clinical and experimental. 2014;63(2):233-41.
67. Kafatos A, Verhagen H, Moschandreas J, Apostolaki I, Van Westerop JJ. Mediterranean diet of Crete: foods and nutrient content. Journal of the American Dietetic Association. 2000;100(12): 1487-93.