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Relationship between Mediterranean diet and asymptomatic peripheral arterial disease in a population of pre-menopausal women

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Abstract *Background and aims:* The Mediterranean Diet (MedD) is considered a very healthy diet useful in the prevention of cardiovascular disease. The present study aims to evaluate adherence to MedD in unselected premenopausal women and its relation with ankle-brachial index (ABI), an index of preclinical atherosclerosis.
Methods and results: A group of 425 patients (age range 45–54 years) was investigated. They were enrolled only if they were asymptomatic for cardiovascular disease. Nutritional parameters were assessed by a self-administered food frequency validated questionnaire (116 items) completed by an interviewer administered 24 h diet recall. They all underwent ABI measurement. The mean MedD Score was 32.2 ± 6.1 (Q1–Q3 range 26–37) comparing with data from Italian population (46 ± 8.3) was significantly lower. Intake of food categories sources of antioxidants was higher in patients with a greater adherence to Med D and was mainly related to fruit and vegetables. Patients were categorized in quartile according to MedD Score and we evaluate the distribution of ABI index within quartile. 31.4% of women in Q1 (lower adherence to MedD) had an ABI lower than 0.9 compared to 18.3% of women in Q4 (higher adherence to MedD): $p < 0.01$. Obesity was more frequent in Q1 compared to Q4 and in women with lower ABI.
Conclusions: Women with a low MedD Score were more obese and showed instrumental sign of preclinical peripheral atherosclerosis. MedD rich in antioxidants from fruit, vegetables and nuts influenced the development of atherosclerosis and was associated with a lower incidence of asymptomatic atherosclerosis.

Background

The Mediterranean Diet (MedD) is a very healthy diet useful in the prevention of cardiovascular disease (CVD) [1–3]. Several studies suggest that higher intakes of fruit, vegetables, and whole grain are associated to a lower risk of atherosclerosis [2,3]. A possible explanation is a

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reduction in oxidatively modified LDL. Because of their antioxidant properties, carotenoids, vitamin E, and vitamin C might protect against free oxygen radicals and lipid peroxidation. A high intake of carotenoids and vitamins is essentially the result of a diet rich in fruit and vegetables and possibly low in meat product [4,5].

Peripheral arterial disease (PAD) is still underdiagnosed and under-treated throughout Europe. Underdiagnosis is largely attributable to the fact that up to 50% of PAD patients can be asymptomatic [6]. The ankle-brachial index (ABI) is a symptom-independent tool that can be used reliably to evaluate PAD [7,8].

The present study aims to evaluate adherence to the Mediterranean Diet (MedD) and intake of antioxidants from food in unselected premenopausal women and their relation with ABI index.

Methods

A retrospective analysis on a group of 650 women (age range 45–54 years) was performed. Patients were refereed to our clinic from general practitioners for screening and prevention of CVD. We selected women only if they were free of symptoms of PAD, had ABI evaluation and a complete nutritional assessment. We excluded participants with a previous history of cardiovascular disease, (ischemic heart disease, heart failure and stroke), those who did not complete questionnaire, and those who did not undergo ABI evaluation and who did not sign the consent (Fig. 1 Supplemental Material). From the initial group we analyzed data from 425 women.

The Local Ethical Review Board approved study and participants signed an informed consent.

Data collection

Nutritional status was assessed by measuring weight, body mass index (BMI), waist circumference and waist-to-hip ratio [9].

The prevalence of nutritional parameters was assessed by a self-administered food frequency questionnaire (FFQ) with 116 items and completed by an interviewer-administered 7-day diet recall questionnaire on the day of first visit [10].

The food list in the FFQ was Italianized, and foods commonly eaten in the Emilia Romagna region of Italy were added. For each food class color photographs of three different portions were displayed. Portion sizes were chosen according to many years of experience in dietary surveys in various parts of Italy [3,9,11].

Food frequency was evaluated using three categories: daily, weekly and monthly and from 1 to 6 number of times (i.e.: once a day, 3 times a week) and was integrated with specific questions on changes in nutrition habits and lifestyle within the last year.

The Mediterranean score was calculated according to Panagiotakos [12] and included 11 food groups: non-refined cereals (whole bread, pasta, rice, other grain, etc.), fruit, vegetables, legumes, potatoes, fish, meat and meat products, poultry, full fat dairy products (butter, cream, cheese, yoghurt, milk), together with olive oil and alcohol intake. Then the frequency consumption of these foods was assessed by assigning individual ratings (from 0 to 5 or the reverse) in each of the 11 food groups cited above.

According to Panagiotakos, for alcohol evaluation, we assigned score 5 for consumption of less than 300 ml of alcohol/day, score 0 for consumption of more than 700 ml/day and scores 4–1 for consumption of 300, 400–500, 600 and 700 or 0 ml/day (100 ml has 12 g ethanol concentration) respectively [12]. Alcohol intake was also qualitatively assessed: wine, wine during meal, beer, liquor. The score ranges from 0 to 55. Higher values of this diet score indicate greater adherence to the Mediterranean diet. In the Attica Study the mean value of the Med Score was 25.46 ± 2.94 in men and 27.18 ± 3.21 in women and we used these values as references. [12].

MedD score was evaluated in quartiles. The first quartile (Q1) comprised 105 patients with Score 27 ± 4.3, the second quartile (Q2) 107 patients with Score 29.8 ± 3.0, the third quartile (Q3) 107 patients with Score 32.8 ± 3.4 and the fourth quartile (Q4) 106 patients with a Score 34.5 ± 4.8.

A dietician using a database system computed food and nutrient intakes from FFQ and dietary recall. We also investigated the use of nutritive and non-nutritive sweetener that was included in the database.

Caffeine consumption was investigated, and estimated as: number of cups of coffee, type of coffee (espresso, American, decaffeinated, cappuccino), number of chocolate snacks and cola soda drinks usually consumed. We estimated caffeine intake as 1 cup of espresso coffee = 90 mg, 1 cappuccino = 110 mg, 1 cup of American coffee = 160 mg, 1 can of cola soda drink = 42 mg [11].

The nutrient database was compiled from food composition tables [3,11,12]. Antioxidant intake was evaluated by nutrient database that was supplemented with data on total antioxidant concentrations in foods [3].

The value of antioxidants was calculated as the total amount of antioxidants derived from the combinations of individual antioxidants that occur naturally in foods. We also evaluated the percentage of antioxidants from food according to the most well known sources of antioxidants: vegetables, fruits, legumes, coffee, and tea [4].

Smoking was also investigated.

ABI measurement

All patients underwent ABI measurement. The ABI is a simple, noninvasive test, measuring the SBP from both brachial arteries and from both the dorsalis pedis and posterior tibial arteries after the patient has been at rest in the supine position for 10 min by using a Doppler device. The ABI of each leg is calculated by dividing the higher of the dorsalis pedis pressure or posterior tibial pressure by the higher of the right or left arm blood pressure [6,7].

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Statistical analysis

SPSS, V.21.0.1 (SPSS Inc, Chicago, Ill) was used for statistical analysis. Results are presented as mean ± SD or frequency expressed as a percentage. We compared the characteristics of patients of different quartiles by means of one-way analysis of variance for continuous variables and chi-square test for proportions. Association between variables (i.e. adherence to Med diet) was evaluated using analysis of variance (ANOVA) and because of multiple comparisons, we used the Bonferroni correction to account for the increase in type I err. Dietary recall was calculated using a statistical food analyzing program. Multiple linear regression was applied to test the association between the MedD Score and normal ABI, antioxidants intake calculated form 7-days recall, age and coffee consumption after controlling for potential confounders: BMI, Hypertension. A $p < 0.05$ was considered statistically significant.

Results

Clinical characteristics are shown in Table 1. The mean MedD Score was 32.2 ± 6.1 (median score was 29.8; Q1–Q3 range 26–37), comparing with data previously recorded from Italian population (46 ± 8.3) was significantly low [3].

Antioxidants intake calculated from 7 days recall was higher in patients with a greater adherence to Med D and was mainly related to fruit (oranges and orange juice, tomato, berries), vegetables (green large leaf, fennel, celery) and in a lower percentage from wine (Fig. 1).

Abstainers from alcohol were 23% of women, while the 67% reported a low consumption of wine mainly during meals (1 ± 0.6 glass/day). Liquors were occasionally consumed by 12% of women.

The 40% of women consumed tea, and 34% were habitual high consumer of coffee (more than 4 cups/day of espresso coffee). However intake of antioxidants from these beverages was low compared to that from vegetables and fruit (Fig. 1).

Patients were categorized in quartile according to MED D Score and we evaluated the distribution of ABI index within quartile. 31.4% of women in Q1 (lower adherence to MedD) had an ABI lower than 0.9 compared to 18.3% of women in Q4 (higher adherence to MedD): $p < 0.01$ (Fig. 2). The second and third quartile has a similar percentage.

BMI and waist circumference were significantly increased in Q1 compared to Q4 (Table 1) and in women with lower ABI. ABI was correlated with MedD Score (rho = 0.41, $P < 0.05$), indicating that lower adherence to the MedD was associated with reduced ABI values suggesting asymptomatic PAD. Women with Mediterranean Score in the highest quartile had lower probability of developed peripheral arterial disease compared with women in the lowest quartile (OR 0.9; 95%CI 1.36–2.2, $p < 0.01$).

Furthermore, participants in the lowest quartile of the diet score had higher body mass index, higher systolic blood pressure (Table 1). No associations were found between diet score and current smoking. However, residual confounding may exist. Thus, the unadjusted analyses were repeated after controlling for age, and body mass index. The results showed that women with very close adherence to MedD had normal ABI compared to those who were away form Mediterranean Diet. Table 2 shows the results from a multiple linear regression models and illustrates the association of MedD Score on ABI value, by dietary habits, after adjustments for BMI and systolic blood pressure.

Discussion

This retrospective analysis was performed to evaluate the relationship between nutritional habits in pre-menopausal age and asymptomatic PAD. We found a low adherence to MedD in women in pre-menopausal age compared to general population and also compared to Greek population [3,12,13].

MedD with high carbohydrates levels and rich in antioxidants from fruit, vegetables and nuts influenced the development of atherosclerosis and were associated with a lower incidence of atherosclerosis in several studies [1].

The PREDIMED study showed a reduction in PAD associated with the Mediterranean diet. This trial tested the effect of the Mediterranean diet enriched with olive oil or dry nuts in 7477 participants with type 2 diabetes mellitus or at least 3 cardiovascular risk factors, and without clinical PAD or baseline CVD. Participants were assigned to one of the following dietary interventions: 1) Integrated Mediterranean diet with extra virgin olive oil; 2) Mediterranean diet supplemented with nuts; 3) low-fat diet (control group). Both Mediterranean diet

Table 1 Clinical characteristics of patients.

Clinical characteristics	Q1	Q2	Q3	Q4
Number of patients	105	107	107	106
Mean age (years)	57 ± 5	56 ± 6	57 ± 4	57 ± 5
Weight (Kg)	90.4 ± 5.2	87.2 ± 5.1*	85.7 ± 4.6*	75.9 ± 6.0**
Body mass index (mean)	29.4 ± 4.0	24.7 ± 2.5*	23.2 ± 3.8*	21.9 ± 4.3*
Waist circumference (cm)	104 ± 5	90 ± 2*	87 ± 7**	86 ± 6**
Systolic blood pressure (mmHg)	131 ± 24	129 ± 21	128 ± 18	125 ± 23*
Diastolic blood pressure (mmHg)	85 ± 10	82 ± 18	80 ± 9	80 ± 12

Significantly different from 1st quartile (Bonferroni correction for multiple comparisons); *$p < 0.05$ versus Q1; **$p < 0.01$ versus Q1.

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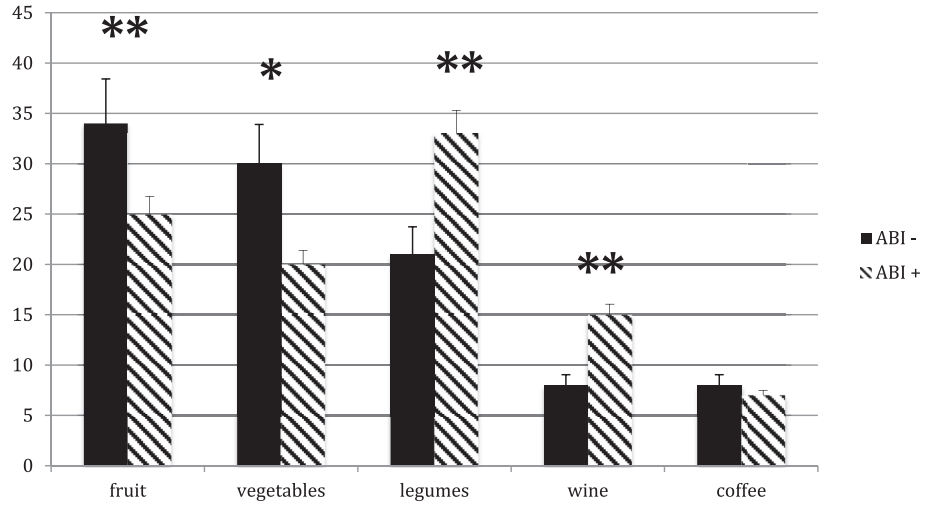

Figure 1 Source of antioxidants derived from dietary recall. Comparison between patients with normal ABI (negative) and pathological ABI (positive). Data are expressed in percentage. *p < 0.05; **p < 0.01.

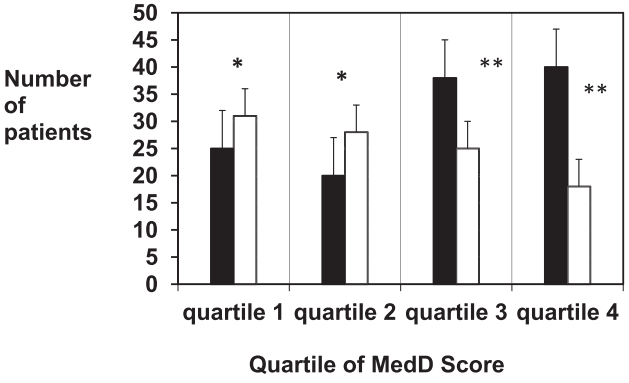

Figure 2 Comparison between normal ABI (dark bar) and low ABI (white bar) according to quartiles of Med D score. *p < 0.05; **p < 0.01.

interventions were associated with a lower risk of PAD compared to control group [14,15].

A recent study reported that consuming a healthier diet was associated with 26% lower likelihood of having high-risk ABI level, after controlling for the traditional cardiometabolic risk factors prevalent in the Hispanic/Latino population [16].

In the present study women in the low quartiles of MedD Score had a greater BMI and a greater waist circumference compared to women in the highest quartile of MedD Score and showed a lower values of ABI. The relationship between obesity and MedD diet has been previously described as well as the association between obesity and pre-clinical PAD [17,18].

Previous studies have largely reported positive associations between central obesity, but not general obesity, with the presence of PAD (thus, negative correlations with ABI); though the association between BMI with PAD is less clear [19–21]. Data of the present study confirm this hypothesis: patients with low MedD score had a greater waist circumference suggesting central obesity. The great majority of studies focused on Metabolic syndrome, however patients with metabolic syndrome were excluded from this study and results referred to obesity evaluated using BMI and waist circumference [22,23].

The Mediterranean lifestyle is characterized by high intake of antioxidants from vegetables and fruit and a smaller intake from wine [4,24,25]. We found that women in the highest quartile of adherence were used to drinking wine during meals. The synergistic effect of drinking wine during meals and bioavailability of antioxidants is well known and is a characteristic of Med Diet [26]. Due to the well known beneficial effects of antioxidants on atherosclerosis we can hypothesize that a low adherence to Med Diet can facilitate the development of atherosclerosis as well as obesity can [4,16,27,28]. Both mechanisms are feasible and lead to atherosclerosis.

Moreover, nutrigenomic studies revealed that the MedD has a protective effect on the expression of several proatherogenic genes involved in vascular inflammation,

Table 2 Results from multiple linear regression analysis evaluating association between quartile of Med Score and other parameters (data expressed Beta coefficient ± SE).

Quartile of MedD	Q1	Q 2–3	Q4	p Q1–Q4
Normal ABI	1.35 ± 0	1.1 ± 1.7	2.9 ± 1.2	0.001
Antioxidant intake from 7 days recall	1.63 ± 1.89	0.13 ± 1.6	3.5 ± 1.01	0.001
Age	−0.14 ± 0.3	−0.21 ± 0.4	−0.16 ± 0.5	Ns
Coffee (<2 cups day)	0.73 ± 0.12	0.54 ± 0.23	0.70 ± 0.17	Ns

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foam cell formation, and thrombosis [29,30]. The MedD can also exert health benefits through changes in the overall transcriptomic response of genes related to cardiovascular risk [30]. CVD protection by the MedD can be explained by a beneficial impact on old and new cardiovascular risk factors, as well as nutrigenomic effects promoting antiatherogenic gene expression [30].

Limitation of the study

The major limitation of the study was the calculation of antioxidants that was performed from data obtained from a validated questionnaire, we did not measured plasmatic levels. Alcohol consumption was derived from self-administered questionnaire and it is possible that was underestimated. Results belong to pre-menopausal women so cannot be translate to general population. Obesity was derived from BMI and waist circumferences, no more evaluation were performed. Data on adiponectin and inflammatory parameters were missing in the great majority of women and would be interesting to understand mechanisms and relationship with obesity. In addition there was a small difference in systolic blood pressure among quartile of MedD and this could influence results.

Conclusions

In conclusion, can be suggests that Mediterranean Diet is a part of a good lifestyle for prevention of atherosclerosis in pre-menopausal women. Some population studies are on going on this topic and will help us to better understand this relationship.

Conflicts of interest

No conflict of interest.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.numecd.2017.09.011.

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