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# The Relation between Mediterranean Diet Score and Coronary Artery Diseases: Dietary Patterns among Coronary Tunisian Patients

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**Abstract**

**Background:** In this study, we not only assessed the association between the adherence to the Mediterranean diet (MD) and Coronary Artery Diseases (CAD), but also we tested how this association depends of gender in coronary Tunisian patients.

**Methods:** The study included 428 patients (292 with CAD and 136 without CAD) who underwent elective coronary angiography in the Cardiology Department. CAD severity was determined by Gensini score. Dietary intake was assessed using a Food Frequency Questionnaire (FFQ) and the adherence to the MD was evaluated by the MD score (MDS).

**Results:** MDS was significantly lower in women with CAD. Women with CAD that present the highest quartile of MDS had a lower risk of CAD before and after adjustment for diabetes, hypertension and obesity. The risk of CAD decreased with a high intake of fruit and vegetables, fish, olive oil, and fruit only for women.

**Conclusion:** The adherence to vegetables, fish and olive oil's diet pattern could favorably affect CAD's risk because of their protective effect particularly in women. Also, MDS could be used to evaluate the nutritional status of patients and to assess other clinical and basic research.

**Keywords:** Mediterranean Diet Score; Coronary Artery Diseases; Cardiovascular Risk Factors

## Abbreviations

MDS: Mediterranean Diet Score; CAD: Coronary Artery Disease; CVD: Cardiovascular Disease; FFQ: Food Frequency Questionnaire

## Introduction

Coronary Artery Disease (CAD) is a common chronic illnesses and one of the leading causes of death [1]. The prevalence of CAD varies considerably around the world with high rates found in the Middle East countries, Africa and the countries bordering the Mediterranean Sea [2]. An epidemiological transition is undergoing in Tunisia and this transition is may be due to ischemic heart disease's risk which is increasing with global life expectancy [3].

The classic cardiovascular risk factor (hypertension, hyperlipidemia, diabetes, smoking and unhealthy lifestyles) are considered among the well-established risk factors for CAD. Otherwise, unhealthy dietary habits may influence the development and progression of CAD [4]. Identical eating habits are traditionally pursued in countries lining the Mediterranean Sea; we count 16 countries that are following similar diet called Mediterranean Diet (MD) [5]. The traditional Mediterranean dietary pattern is characterized by high plant-based dietary sources, based on a very important consumption of fruits and vegetables, cereals including bread, potatoes, beans, nuts and seeds. The MD includes also infrequent consumption of red meat and as regards to dairy products, fish, eggs and poultry the consumption was from low to moderate [6,7]. The traditional MD is well known for its cardio-protective effects [8,9] and has already been reported to be inversely associated to cardiovascular risk factors and precursors of Cardiovascular Disease (CVD). In fact, studies have shown that compliance with MD could prevent inflammation and this finding may explain its important role in atherosclerosis physiopathology and in cardiovascular disease [10,11]. In addition, it have been shown that elevated compliance with MD could, over time, decrease atherosclerosis in coronary arteries [12,13]. Furthermore, the existent difference of nutrition and eating habits between both sexes has been the interest of investigations for years. Research, in the nutrition field revealed that women diet and try weight loss practice more than men [14]. In this study, we assessed both the association between the MD and CAD and how it depends on gender.

## Methods

### Patients

We collected 428 patients who underwent elective coronary angiography in the Cardiology Department of "Rabta Hospital" (Tunis-Tunisia) by an experienced cardiologist. Those patients are divided into 2 groups (292 with CAD (CAD+) and 136 without CAD (CAD-). Patients with a history of neoplastic, hepatic, renal, cerebral,




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**Table 1:** Clinical and biochemical of patients without and with CAD.

| | Total N=428 | | |
|---|---|---|---|
| | CAD- N=136 | CAD+ N=292 | p |
| Gender (Male/Female) | 70/66 | 196/96 | <0.01 |
| Age (years), mean (SD) | 53.15 (7.87) | 57.38 (7.63) | <0.01 |
| Body mass index (kg/m$^2$), mean (SD) | 28.55 (5.04) | 27.51 (4.84) | 0.05 |
| Systolic blood pressure (mmHg), mean (SD) | 136.68 (22.64) | 135.35 (21.67) | 0.58 |
| Diastolic blood pressure (mmHg), mean (SD) | 80.69 (13.38) | 78.17 (12.03) | 0.06 |
| Hypertension (%) | 65.70 | 76.70 | 0.02 |
| Diabetes (%) | 44.60 | 70.00 | <0.01 |
| Obesity (%) | 35.30 | 24.50 | 0.03 |
| Dyslipidemia (%) | 18.10 | 26.30 | 0.07 |
| Smoking (%) | 18.80 | 16.20 | 0.32 |
| Fasting blood glucose (mg/dL), mean (SD) | 116.58 (35.85) | 142.59 (68.08) | 0.01 |
| Total cholesterol (mg/dL), mean (SD) | 187 (42.74) | 189 (50.62) | 0.32 |
| LDL- cholesterol (mg/dL), mean (SD) | 110.50 (34.7) | 119.36 (42.97) | 0.09 |
| HDL- cholesterol (mg/dL), mean (SD) | 43.63 (13.88) | 39.14 (12.97) | <0.01 |
| Triglyceride (mg/dL), median (25$^{th}$-75$^{th}$) | 105 (86-150.2) | 142 (102.5-184.7) | <0.01 |
| Gensini score, median (25$^{th}$-75$^{th}$) | 0 | 16.25 (5.5-35.5) | <0.01 |
| **Drug therapy received** | | | |
| Angiotensin converting enzyme inhibitor (%) | 51.4 | 84 | <0.01 |
| $\beta$-blocker (%) | 48.6 | 79.6 | <0.01 |
| Diuretics (%) | 11.4 | 15.8 | 0.37 |
| Statin (%) | 38.6 | 78.6 | <0.01 |
| Fibrate (%) | 18.9 | 12.4 | 0.23 |
| Insulin (%) | 29 | 42.5 | 0.11 |
| Oral anti-diabetic (%) | 61.3 | 53.4 | 0.27 |
| Aspirin (%) | - | 67.4 | - |
| Other antiplatelet drugs (%) | - | 46.4 | - |

infections or autoimmune disease, valvular heart disease, peripheral atherosclerotic disease, dysfunction and myocardial infarction in less than 72 hours or any surgical procedure in the preceding six months, were excluded from this study [15].

## Clinical and Biological Data

Blood pressure was recorded as the average of two measurements (systolic blood pressure and diastolic blood pressure) after 15 minutes of rest and measured at mercury millimeter. After fasting overnight, blood specimens were collected into heparin and sodium fluoride containing tubes. Blood samples were centrifuged at 1500 g for 20 minutes. Then analyzes were performed within 4 hours. All biochemical analyses (serum levels of fasting blood glucose, total cholesterol, triglyceride and High-Density Lipoprotein cholesterol (HDL cholesterol)) were resolved by enzymatic methods using a Hitachi 912 analyzer (Roche). Low-Density Lipoprotein cholesterol (LDL- cholesterol) was estimated by the Friedewald formula.

## Food-Frequency Questionnaire and Mediterranean Diet Score

Dietary intake of study patients were assessed using a Food Frequency Questionnaire (FFQ) validated and adapted to the Tunisian context [16]. The Mediterranean Diet Score (MDS), was used to calculate the Mediterranean pattern and this score have been elucidated previously by Martinez-Gonzalez et al [17]. Nine parameters were included in this score. The resulting score ranged from 0 to 9 points and it was developed to predict quantitively the bond linking the cardio-protective elements of the Mediterranean diet [17].

## Angiographic Assessment

All patients underwent coronary angiography, using standard techniques. The angiographic features, which included the location of the lesion and the percentage of stenosis, were obtained by scanning angiography. The severity of CAD was assessed by the Gensini score [18], a validated method, which grades narrowing of the coronary artery lumen as: 1 (1-25%), 2 (26-50%), 4 (51-75%), 8 (76-90%), 16 (91-99%) and 32 (100%) complete occlusion. Each segment is followed by a multiplying factor from 0.5 to 5 depending on the functional significance of the area supplied by that segment [18]. The results of coronary angiography were resolved in the opinion consensus of two experienced interventional cardiologists. Patients

CAD + were defined by a Gensini score > 0 [15].

### Statistical Analysis

Data entry screens including quality checks, as well as validation by double entry, used EpiData Software version 3.1 [19]. Statistical analysis was performed using the SPSS version 18.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to verify the normality of the distribution of continuous variables. These variables were compared using parametric tests (Student t test) or nonparametric tests (Mann-Whitney test). Quantitative variables were presented as mean values (Standard Deviations (SD)) and median ($25^{th}$-$75^{th}$). Categorical variables were shown as percentages (Pearson Chi-square test). Binary logistic regression analysis (unadjusted and multi-adjusted) was used to evaluate Mediterranean Diet Score on the CAD. The association between the food consumption and CAD was tested by binary regression analysis after adjustment by diabetes, hypertension and obesity according to gender. In all analyses, $p<0.05$ was considered statistically significant.

## Results

Table 1 summarizes the clinical and biological characteristics of the two groups; 428 patients (Men 256 and women 172) were enrolled in the present study. Patients with hypertension and diabetes were significantly higher in the CAD+ than in the CAD- group ($p< 0.05$) (Table 1). The proportion of smokers and dyslipidemia showed no difference between the CAD- and CAD+ groups (Table 1). The mean intake of the 9 food indexes used to construct the MDS by Martinez Gonzalez among without and with CAD is shown in Table 2. We noticed that women with CAD consumed significantly less of fruits, fruits-vegetables and fish. Moreover, MDS is significantly higher in women without CAD (4.00 (1.62) *vs* 3.51 (1.57); p=0.04). Whereas MDS is not significant in men between the 2 groups. Obviously, MDS was also significantly higher in women without CAD when CVD factors were absent (Figure 1a). In binary logistic regression analysis, women without CAD in the highest quartile of MDS have a lower risk of CAD before and after adjustment for diabetes, hypertension and obesity. This difference is borderline significant (Figure 1b). Figure 2 presents a binary logistic regression analysis of food consumption in CAD according to gender after adjustment for diabetes, hypertension and obesity. According to the outcomes, the risk of CAD decreased in association with high intake of fruit and vegetables, fish, olive oil, and fruits only for women (Figure 2).

## Discussion

In this study, the relation between MDS and CAD showed that MDS was significantly lower only in women with CAD. Indeed, these women with CAD consume noteworthy less of fruit, fruits-vegetables, fish and meat. But for male there wasn't a noticeable difference between the groups of patients with and without CAD. The differences in both sex in response to diet were investigated in only few studies. They found that women replied differently to diet in comparison to men. Observed differences in men and women were related more to sex than to gender differences [20] and this difference is due to hormones [21,22]. In fact, sex-related factors such as sex hormones influenced the impact of diet on measured metabolic changes and this impact isn't influenced by diet adherence which is modulated by gender-related factors [23]. In addition, some studies have shown that the adoption of an MD had a more cardio-protective effect in women than in men [24,25] besides, those, persons with high intakes of fruits, vegetables, experience of olive oil had a lower risk of CAD [26-27]. Using MDS leads us to develop a simple dietary score, build on inherent characteristics of the MD. Recently, the analysis of eating habits has appeared as an alternative and complementary approach to the consideration of the relation between diet and various chronic diseases risk including CAD. Indeed, life habits have long been correlated with lower CVD [28]. Particularly, the MD has been related to better health, reduced mortality from all causes and protection effects and improver on chronic diseases [29-31]. More

**Table 2:** Analysis of food frequency in MDS in men and women based on CAD.

| | | Total N=428 | | | Men N=256 | | | Women N=172 | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | CAD- | CAD+ | p | CAD- | CAD+ | p | CAD- | CAD+ | p |
| Olive oil (servings/day) | | 1.83 (1.67) | 1.84 (1.50) | 0.91 | 1.74 (1.66) | 1.95 (1.56) | 0.39 | 1.91 (1.69) | 1.61 (1.33) | 0.06 |
| Fruit (servings/day) | | 1.26 (1.02) | 1.12 (0.95) | 0.17 | 1.23 (0.98) | 1.22 (0.97) | 0.96 | 1.29 (1.06) | 0.92 (0.88) | 0.01 |
| Vegetables or Salad (servings/day) | | 0.75 (0.63) | 0.77 (0.80) | 0.73 | 0.71 (0.72) | 0.77 (0.79) | 0.62 | 0.78 (0.79) | 0.78 (0.83) | 0.97 |
| Fruit and Vegetables (servings/day) | | 1.74 (1.15) | 1.60 (1.05) | 0.23 | 1.70 (1.10) | 1.72 (1.08) | 0.89 | 1.77 (1.19) | 1.34 (0.95) | 0.01 |
| Legumes (servings/week) | | 0.63 (0.88) | 0.60 (0.91) | 0.75 | 0.67 (1.03) | 0.64 (0.96) | 0.85 | 0.60 (0.75) | 0.51 (0.80) | 0.49 |
| Fish (servings/week) | | 1.20 (1.19) | 1.08 (0.94) | 0.27 | 1.18 (1.26) | 1.20 (0.99) | 0.92 | 1.21 (1.14) | 0.82 (0.79) | 0.01 |
| Meat (servings/day) | | 1.49 (0.47) | 1.61 (0.66) | 0.09 | 1.53 (0.48) | 1.59 (0.71) | 0.49 | 1.40 (0.44) | 1.62 (0.62) | 0.01 |
| Cereals (servings/day) | | 3.10 (1.08) | 3.18 (0.97) | 0.48 | 3.31 (1.30) | 3.21 (0.88) | 0.52 | 2.94 (0.86) | 3.12 (1.12) | 0.28 |
| Alcohol (glasses/day) | | 0.88 (1.51) | 0.94 (1.47) | 0.79 | 0.88 (1.51) | 0.94 (1.47) | 0.79 | - | - | - |
| Mediterranean Diet Score | Median ($25^{th}$-$75^{th}$) | 4 (3-5) | 4 (2-5) | 0.22 | 3 (2-4.25) | 4 (2-5) | 0.41 | 4 (3-5) | 4 (2-5) | 0.03 |
| | Mean (SD) | 3.72 (1.65) | 3.45 (1.58) | 0.13 | 3.21 (1.71) | 3.46 (1.57) | 0.30 | 4.00 (1.62) | 3.51 (1.57) | 0.04 |

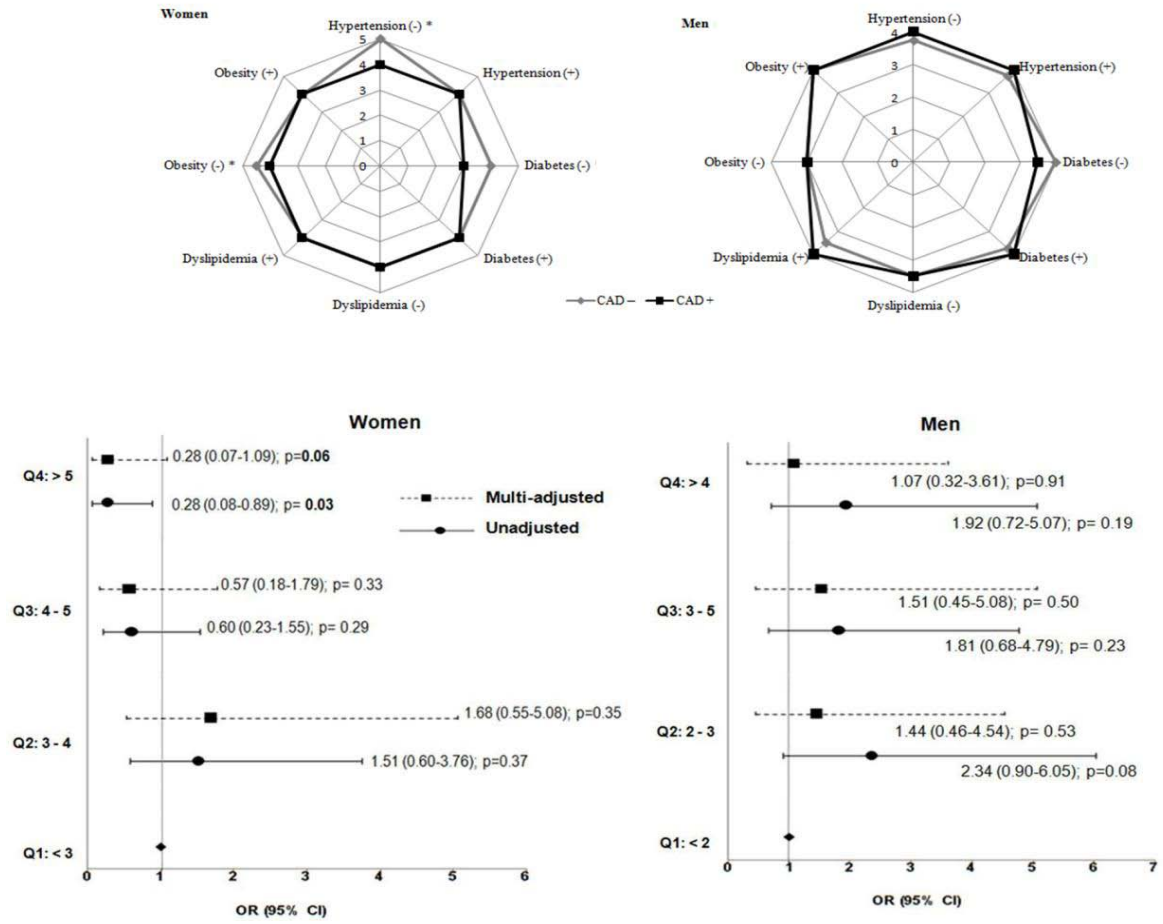


**Figure 1:** MDS according to cardiovascular risk factor in men and women. **(a)** Radar chart of MDS, **(b)** unadjusted and multi-adjusted (adjusted by diabetes, hypertension and obesity*)* Odd Ratios (ORs) with 95% Confidence Intervals (CI) of CAD by quartiles MDS. *p<0.05

specifically, this type of diet have been related to benefits regarding cardiovascular risk factors such as hypertension, diabetes, obesity and metabolic syndrome [32,33,8]. In the present study and according to cardiovascular risk factors, we found a MDS increase in women without CAD than women with CAD when theses did not present a risk factor. Moreover, after adjustment for cardiovascular risk factors, women had a lower risk of CAD especially in the last quartile. The differences that reside between both men and women regarding the dietary pattern in few studies highlights the possible role of nutritional habits in gender differences confronted in CAD [34,35]. In the last decade, several attempts were made to differentiate the lifestyle and specific dietary factors that could elevate cardiovascular risk. Indeed, risk factor's frequency and characteristics in women with CAD were different from those of men. Actually, women have modifiable risk factors which are related to lifestyle habits, such as obesity and physical inactivity [36-39].

On the other hand, similar to other works, the results of CAD risk decreased in association with high intake of vegetables, fish, olive oil and fruit [26,27]. Antioxidants in the basic MD structure are thought to contribute particularly to the cardio-protective effect. It is known that vegetative nutrients and olive oil, particularly rich in antioxidants, are important elements in this context. Natural antioxidants like carotenes, tocopherols and phenolic compounds reserves fatty acids constituting olive oil [40]. It is considered that structure rich in polyphenols nitric oxide plays a major role in preserving endothelial function. Experimental studies demonstrated that polyphenols in olive oil have an anti-inflammatory and anti-atherogenic effects [41,42]. The application of MDS in epidemiological studies has yielded conflicting results [26]. It could be explained by the limitations of diet scores such as the subjectivity related with food products are included with each score and how each component is marked. The studied score could lack food items which define food habits of studied population. Another explanation for the conflicting findings is that traditional food preparation methods are not the same and influence greatly inside and between countries.

## Conclusion

In conclusion, our findings suggest that adherence to vegetables; fish and olive oil's diet pattern could favorably affect CAD's risk because of their protective effect particularly in women. Thereby, when healthy food variety are combined into a dietary pattern, the estimated obtained effect is larger despite the weak individual which suggests that they act in the same way to give a significant reduction in CAD risk. Also, MDS could be used to evaluate the nutritional status of patients and to assess other clinical and basic research.

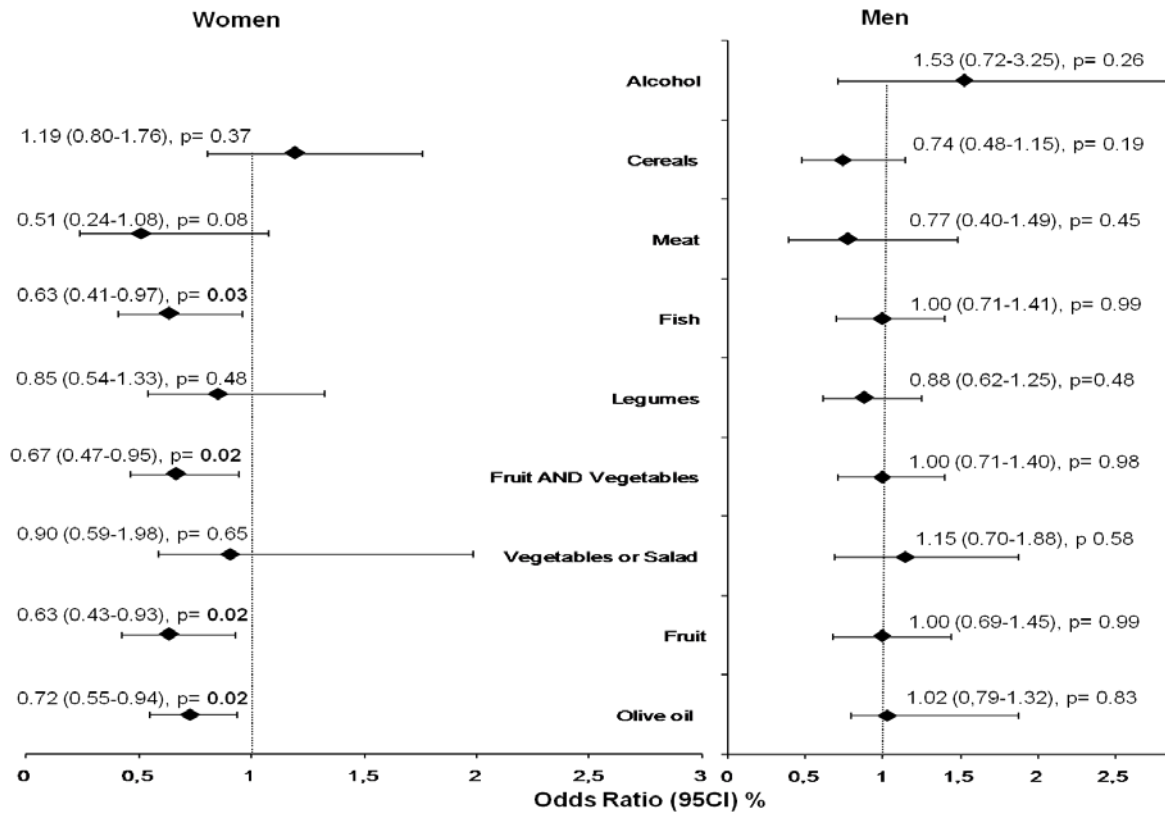


**Figure 2:** Binary logistic regression analysis of food consumption in CAD according to gender after adjusted by diabetes, hypertension and obesity.

## Limitations

Since it is a cross-sectional study, it is impossible to establish a causal relationship due to the lack of information of follow-up of analyzed subjects that underwent a single coronary angiogram. The study sample was quite small, despite the fact that it has been larger in other studies and our findings are only operative to populations like ours, because traditional food preparation methods vary and influence greatly inside and between countries.

## Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Rabta Hospital and informed consent was obtained from all participants of this study. This work was carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

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