Research Article

HEALTHY MEDITERRANEAN DIET AND CARDIOVASCULAR DISEASE: RETROSPECTIVE ELDERLY SAMPLE IN THE JOINT ANALYSIS OF CARDIOPATHY, DRUGS AND MEDITERRANEAN DIET

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ABSTRACT

Introduction: Cardiovascular disease is the leading global cause of death. Dietary habits are changing rapidly with alarming rates of obesity. Adherence to the Mediterranean diet and cardiovascular risk are inversely correlated. Prevention of CVD emphasizes, apart from lifestyle changes, the use of drugs.

Objective: Describe the relationship between CVD, the MD and CVD drugs intake. Study the differences between men and women in a group of elderly in the Community of Madrid.

Methods: Case-control study conformed of 342 subjects. Anthropometric measurements and dietary assessment using the PREDIMED score were obtained.

Results: CVD diagnosis and CVD-drugs consumption were higher in women. Besides, higher adherence (in percentage) to MD was observed in men, while higher PREDIMED scores (mean) were registered in women. No statistically significant differences were found when analyzing the dependence between sex, CVD-drugs consumption and CVD presence, and adherence to the MD and the PREDIMED score.

Conclusion: CVD diagnosis, drug consumption and PREDIMED score was higher in women, although men showed better adherence to MD. There were no significant differences between cases and control in the analysis of adherence to MD and diagnosis/CVD drug consumption. Growing evidence indicates that MD is beneficial to human health, fact not observed in our sample.

INTRODUCTION

Cardiovascular disease (CVD) is the leading global cause of death (Benjamin *et al*. 2017), accounting for 17.7 million deaths in 2015, comprising 31% of total global deaths. Of these deaths, an estimated 7.4 million were due to coronary heart disease and 6.7 million were due to stroke (WHO 2017).

CVD remains the main cause of mortality in Europe (Banegas *et al*. 2011), it causes more than half of all deaths across the European Region (World Health Organization 2017). The European Study on Cardiovascular Risk Prevention and Management in Usual Daily Practice (EURIKA) (Rodríguez-Artalejo *et al*. 2010) was a cross-sectional study conducted simultaneously in 12 European countries to attempt a large-scale comparative assessment of the status of primary CVD prevention among patients with varying degrees of CVD risk across Europe. The EURIKA study showed that: (i) many patients with treated CVD risk factors remains inadequately controlled, (ii) a large proportion of patients achieving treatment goals for individual risk factors remain at high-residual CVD risk, and (iii) lifestyle interventions are generally not well implemented.

Although the incidence of coronary and cerebrovascular disease mortality has declined during recent decades, CVD is

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still also the leading cause of death (34.7% of total deaths (Haro *et al.* 2014)) and disability in Spain (Amor *et al.* 2015).

CVD is mediated by several antecedent behavioural risk factors, and its onset might be prevented or delayed by altering one or several risk factors (Alageel *et al.* 2017).Those risk factors comprise tobacco use, unhealthy diet and obesity, physical inactivity and harmful use of alcohol (WHO 2017).

While in former years large proportions of the population adhered to a Mediterranean diet (MD), dietary habits are changing rapidly with alarming rates of obesity (Haro *et al.* 2014).

The traditional MD is characterized by a high intake of olive oil, fruit, nuts, vegetables, and cereals; a moderate intake of fish and poultry; a low intake of dairy products, red meat, processed meats, and sweets; and wine in moderation, consumed with meals (Estruch *et al.* 2013).

Observational cohort studies (Sofi *et al.* 2010; Serra-Majem, Roman, and Estruch 2006) and a secondary prevention trial (the Lyon Diet Heart Study) (de Lorgeril *et al.* 2009), have shown an inverse association between adherence to the MD and cardiovascular risk (Estruch *et al.* 2013), and a systematic review ranked the MD as the most likely dietary model to provide protection against coronary heart disease (Mente *et al.* 2009).

As no randomized controlled trial was ever conducted to assess to what extent a MD offers greater benefits than a usual diet in the primary prevention of cardiovascular events, the PREDIMED study (PREDIMED meaning *PREvención con DIeta MEDiterránea*) was designed to test the effects of a MD intervention on prevention of CVD (Estruch *et al.* 2013).

Recent guidelines on primary and secondary prevention of CVD emphasize, apart from lifestyle changes, the use of cardiovascular drugs, in particular platelet aggregation inhibitors, lipid-lowering drugs (mostly statins), and blood pressure-lowering drugs [including beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blockers and diuretics (Koopman *et al.* 2013). Several studies have indicated that in secondary prevention, age and gender inequalities exist in the use of preventive drugs (Lahoz *et al.* 2009; Tjia *et al.* 2010). These points towards less lipid-lowering drug use at older ages and in women. Data for primary prevention are much more limited and seem to point towards differences in cardiovascular drug use with increasing age, in particular lipid-lowering drugs lagging behind blood pressure-lowering drugs (Sheppard *et al.* 2012).

Objective

Describe if there is a relationship between CVD, the MD and the intake of drugs for CVD.

Study the differences between men and women in a group of elderly in the Community of Madrid (Spain).

METHODS

Study Population

A Case-Control study was conducted. The initial study population was constituted by 342 subjects, of both sexes, from the Community of Madrid in 2016-2017. Mean age (± standard deviation) was 75.22 ± 6.47 years old. Inclusion criteria were subjects over 65 years old, of both sexes, who agreed to participate voluntarily and filled in the informed consent. Participants who did not meet inclusion criteria (n=38), complete all questionnaires or were absent on the day of the survey were excluded. Study population was finally constituted by 304 subjects. Declarations of Helsinki ethical priniciples (WMA 2013) were followed and the rights of the all participants respected. All subjects signed an informed consent to participate in the project.

Study factors

Anthropometric measurements: Weight, height, BMI and waist circumference of each participant was measured (Table I). Weight and BMI were determined through an electrical bioimpedance, tetra-pole, mono-frequency (50 kHz), Tanita BP601 Model; and a flexible non-elastic, metallic measuring tape, ranged from 0.1mm to 150cm was used to measure waist circumference. Height was measured with a SECA mobile rod height meter with precision of 1 mm, according to the WHO protocol (World Health Organization 2008).

Table I Personal and anthropometric data of the sample

	Total	Men	Women
	Mean ± SD	Mean ± SD	Mean ± SD
Age (years)	75.22 ± 6.47	75.01 ± 5.65	75.29 ± 6.74
Weight (Kg)	70.36 ± 12.81	77.1 ± 12.09	67.68 ± 11.73
Height (m)	1.56 ± 0.86	1.66 ± 0.65	1.53 ± 0.68
BMI (Kg/m^2)	28.67 ± 4.59	28.09 ± 3.7	28.76 ± 4.74
Weist circumference (cm)	96.55 ± 13.63	102.63 ± 11.62	94.1 ± 13.43

Dietary assessment: the PREDIMED was used to assess adherence to the MD. The PREDIMED study was a primary prevention randomized clinical trial designed to test the hypothesis that the MD would be superior to a low-fat diet for CVD protection. Dietitians used a specific tool to both evaluate adherence to the MD: a validated 14-point Mediterranean Diet Adherence Screener (MEDAS) (Schröder H, Fitó M, Estruch R, Martínez-González MA, Corella D, Salas-Salvadó J, Lamuela-Raventós R, Ros E, Salaverría I, Fiol M, Lapetra J, Vinyoles E, Gómez-Gracia E, Lahoz C, Serra-Majem L, Pintó X, Ruiz-Gutierrez V, Covas MISchröder H1, Fitó M, Estruc 2011). The MEDAS consists of 12 questions on food consumption frequency and 2 questions on food intake habits considered characteristic of the Spanish MD. Each question was scored 0 or 1. One point was given for using olive oil as the principal source of fat for cooking, preferring white meat over red meat, or for consuming: 1) 4 or more tablespoons (1 table spoon = 13.5 g) of olive oil/day (including that used in frying, salads, meals eaten away from home, etc.); 2) 2 or more servings of vegetables/day; 3) 3 or more pieces of fruit/day; 4) ,1 serving of red meat or sausages/day; 5) ,1 serving of animal fat/day; 6) ,1 cup (1 cup = 100 mL) of sugar-sweetened beverages/day; 7) 7 or more servings of red wine/week; 8) 3 or more servings of legums/week; 9) 3 or more servings of fish/week; 10) fewer than 2 commercial pastries/week; 11) 3 or more servings of nuts/week; or 12) 2 or more servings/week of a dish with a traditional sauce of tomatoes, garlic, onion, or leeks saute´ed in olive oil. If the condition was not met, 0 points were recorded for the category. The final PREDIMED

score ranged from 0 to 14. Good/moderate adherence to de MD is considered score >9.

Medical history: an *ad hoc* survey which included history of illness and CVD drug consumption was fulfilled.

Data were collected by trained and formed nutritionists and dieticians, standardizing the data collection protocol and monitoring the study.

For the statistical analyzes, a joint and separate analysis was performed between subjects having CVD or taking drugs for CVD (considered as study subjects), and those who did not have CVD and did not take drugs for CVD (considered as controls).

Statistical analysis

The statistical analysis entailed descriptive analyses, presenting the results in means, standard deviation and percentages. We used parametric statistical tests such as Student's t-test to analyse the differences between the means in two groups of quantitative variables and a Chi-square test for non-parametric qualitative variables. A value of $p < 0.05$ was considered a significant difference. Analysis of the data collected was processed with system SPSS® (version 20).

RESULTS

The sample consisted of 304 people, 72.8% women and 27.2% men, aged 75.22 ± 6.47 years. (Table I). There were no statistically differences in baseline variables between participants.

Table II/Figure 1 shows the percentage of participants who were diagnosed with CVD and consumed specific drugs for the disease. Both diagnosis and consumption were higher in women. Besides, higher adherence (in percentage) to MD was observed in men, while higher PREDIMED scores (mean) were registered in women. *P-values* of the chi-squared tests are also shown for each variable. No significant diference where obtain between groups.

Table II Descriptive data on CVD drug consumption and diagnostic, and PREDIMED score.

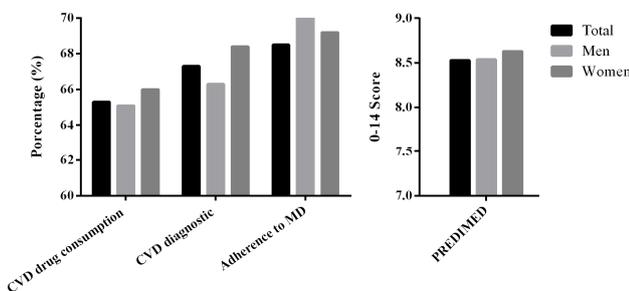|	Total	Men	Women	*p-value*
CVD drug consumption (%, yes)	65.3	65.1	66.0	0.883
CVD diagnostic (%, yes)	67.3	66.3	68.4	0.725
PREDIMED (score)	8.53 ± 2.45	8.54 ± 2.39	8.63 ± 2.38	0.761
Adherence to Mediterranean diet (%, yes)	68.5	70.6	69.2	0.811

Fig 1 Descriptive data on CVD drug consumption and diagnostic, and PREDIMED score (MEDAS).

Table III shows the *p-values* of the chi-squared tests to know the dependence between sex, the consumption of drugs for CVD and the presence of CVD, and the adherence to the MD

and the PREDIMED score (MEDAS). Student's t test for independent samples was performed on all variables. In those whose Levene test was significant, the Mann-Whitney U test (adherence to MD vs. drug consumption, and adherence to MD vs. presence of CVD) was performed.

Table III Relation between adherence to the Mediterranean diet and the PREDIMED score, and drug consumption for CVD and diagnostic.

		Predimed Score ≥ 9		Predimed Score	*p-value*
		Yes	No	Mean ± SD	
CVD drug consumption (%)	Yes	51.2	48.8	8.57 ± 2.15	0.492
	No	55.2	44.8	8.63 ± 2.62	
CVD diagnostic (%)	Yes	49.3	50.7	8.47 ± 2.36	0.128
	No	58.7	41.3	8.83 ± 2.26	

A better PREDIMED score (MEDAS) was observed in the control sample than in the case sample, but with no statistically significant differences ($p > 0.05$).

DISCUSSION

Adherence to MD has a regulating effect on CVD risk factors (i.e., arterial blood pressure, cholesterol levels, insulin resistance, endothelial function and inflammation), although all these effects are linked to an apparent synergy of the entire dietary pattern, rather than being the result of any of its components separately, implying that the Mediterranean dietary pattern should be considered as an entity with respect to disease prevention (Georgousopoulou *et al.* 2017).

Adhering to a Mediterranean style diet was associated with a 39% lower coronary mortality risk and a 29% lower cardiovascular mortality risk in middle-aged and elderly European men and women in the HALE project (The Seven Countries Study 2017). Similar results were obtained in Guasch-Ferré *et al.* study, where MD reduced the incidence of major cardiovascular events by approximately 30% [Hazard Ratio (HR): 0.70 (95% confidence interval, 0.54, 0.92) and 28% [HR=0.72 (0.54, 0.96)] when supplemented with extra virgin olive oil or nuts, respectively, in comparison to the control diet (Guasch-Ferré *et al.* 2017).

Prospective observational studies in many populations showed that lower intake of saturated fat coupled with higher intake of polyunsaturated and monounsaturated fat is associated with lower rates of CVD and of other major causes of death and all-cause mortality. Replacement of saturated with unsaturated fats lowers low-density lipoprotein cholesterol, a cause of atherosclerosis, linking biological evidence with incidence of CVD in populations and in clinical trials (Sacks *et al.* 2017).This can be seen in randomized controlled trials that lowered intake of dietary saturated fat and replaced it with polyunsaturated vegetable oil reduced CVD by ≈30%, similar to the reduction achieved by statin treatment.

The one existing study (Samieri *et al.* 2013) that has investigated the MD with respect to a multidimensional healthy aging model (including absence of disease and disability, good physical and cognitive functioning, and an active engagement with life) has found that a high adherence to the MD, defined as being in the 5th quintile of the Alternate Mediterranean Diet Score, was prospectively related to nearly 50% higher odds for healthy aging. Thus, the MD may have an important preventive

potential with respect to age-related health decline (Assmann *et al.* 2017).

In accord to the previous studies, Dontas *et al.* (Dontas *et al.* 2007) found that greater adherence to the MD was associated with 21% lower odds of having one additional risk factor (ie, hypertension, hypercholesterolemia, diabetes, obesity) in women and with 14% lower odds in men, irrespective of various potential confounders. This finding may be directly linked to the reduction of cardiovascular risk and consequently prolong life span.

The CARDIO2000 investigators focused their interest on hypercholesterolemic patients (Pitsavos *et al.* 2002) they observed a synergistic effect of the combination of the MD with statin treatment on coronary risk. In particular, they observed that the aforementioned combination was associated with a 43% reduction in coronary risk.

A prospective study involving 22,043 adults from Greece (Antonia Trichopoulou *et al.* 2003) found that approximately a 20% increment in the MD score was associated with a 33% reduction in coronary heart disease mortality. These associations were present irrespective of sex, smoking status, level of education, BMI, and physical activity. This is signifi cant among participants 55 years of age or older, but not among younger participants. This age-specific association might reflect the effects of a cumulative exposure to a more healthy diet (ie, the MD). In a review paper, Trichopoulou *et al.* (1995) (A Trichopoulou *et al.* 1995) concluded that the MD is positively associated with longevity among the elderly, and therefore the traditional MD represents a healthy nutritional pattern.

Our findings did not show association between better adherence to the MD with less consumption of cardiovascular drugs, or with less diagnosis of the disease. An important concern, but one that has received less attention, involves changes made once a disease has already been diagnosed. Healthy behaviors following the onset of disease are critical because they can lower the risk of recurrence, reduce severity of disease, increase functioning, and extend longevity. Temporary changes in behavior are unlikely to have substantial effects; permanent changes are necessary to have a meaningful effect on health (Newsom *et al.* 2012).

The basic tenets of several health behavior models suggest that the onset of chronic illness should motivate lifestyle changes. However, patterns of behavior change following diagnosis indicate that the vast majority of individuals diagnosed with a new chronic condition do not adopt healthier behaviours. Latent growth curve analyses up to 14 years after diagnosis, in Newsom *et al.* (Newsom *et al.* 2012) study, showed no average long-term improvement in health behaviors. Similar conclusions were obtained in another study of the same author (Newson *et al.* 2012). Unhealthy behaviors which have been repeated over a lifetime are likely to have become entrenched habits by middle and older age, making them difficult to change even in the face of imminent threats to one's health.

If theoretical notions suggest that lifestyle changes are probable after a diagnosis of a serious illness, better results would be obtained when analyzing healthy behaviour once the patient has obtained the diagnostic.

The existing literature provides an incomplete picture of the extent to which long-term changes are made following a newly diagnosed condition and whether individuals are more likely to make lifestyle improvements in response to certain health conditions. A better understanding of these issues is important to evaluate the theoretical processes involved in illness perception and behavior change as well as to better assess the adequacy of secondary prevention efforts.

CONCLUSION

CVD diagnosis and consumption of drugs for CVD were higher in women. Besides, higher adherence (shown as percentage) to MD was observed in men, while higher PREDIMED scores (MEDAS) (shown as mean) were registered in women. However, it was not observed that to a greater adherence to the MD, there is less diagnosis of CVD or less consumption of drugs for CVD. Further studies are needed in order to corroborate if the MD represents an ideal diet for all age groups, including the elderly, and has an important role in the prevention of metabolic and cardiovascular disease.

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Conflict of Interest

The authors declare no conflict of interests.

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