

Mediterranean diet and metabolic syndrome: a cross-sectional study in the Canary Islands

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Abstract

Objective: Assessment of relation between metabolic syndrome (MS) and Mediterranean diet (MD) adherence.

Design: Cross-sectional study. ATP III definition of MS was used. Adherence to MD was assessed with a Food Frequency Questionnaire. Intakes of cereal, fruit, legumes, vegetables, fish, nuts, monounsaturated to saturated ratio, alcohol from red wine, whole-fat dairy products and red meat were considered.

Setting: Representative sample of population from the Canary Islands (Spain) participating in the Canarian Nutrition Survey (ENCA).

Subjects: 578 adults > 18 years.

Results: Of the subjects, 24.4% presented MS. Once adjusted, MD adherence was not related to MS prevalence, but subjects in the third tertile of adherence presented 70% lower prevalence of the blood pressure criteria and 2.5 times more prevalence of the glycaemia criteria with respect to the first tertile. Red meat intake was associated with higher prevalence of blood pressure criteria. Moderate alcohol intake from red wine was associated with lower prevalence of these criteria in women and lower prevalence of HDL cholesterol criteria in men. Fruit intake showed a protective effect on triglyceride criteria, whereas vegetable intake was associated with higher prevalence of this criterion. Cereals' intake showed a protective effect over insulin resistance measured by high insulinaemia level. Fruit intake showed a significant protective effect over high Homeostasis Model Assessment index. Whole-fat dairy products showed a significant protective effect on the glycaemia criteria. High monounsaturated to saturated fatty acid intake showed a protective effect on insulin resistance.

Conclusions: Some components of the MD showed a protective effect on the MS and its components.

Keywords
Metabolic syndrome
Insulin resistance
Mediterranean diet

Introduction

Cardiovascular diseases are the first death cause in European countries¹. It is well known that hypercholesterolaemia, hypertension, tobacco consumption and other factors increase the risk of developing cardiovascular disease². In Spain, a 'Spanish paradox' has been described³, consisting of a high prevalence of cardiovascular risk factors but low incidence and mortality for ischaemic heart disease⁴. The existence of protective factors in Spanish subjects was considered to be a possible explanation of this paradox. One of the proposed protective factors was a dietary pattern close to the Mediterranean diet (MD). In the Canary Islands, as opposed as to what is found in the rest of Spain, a high prevalence of cardiovascular risk factors coexists with one

of the highest cardiovascular mortality rates of the country⁵. The present paper is intended to clarify some issues concerning dietary habits of the Canarian population that could influence on their cardiovascular morbidity and mortality.

The metabolic syndrome (MS) is a cluster of cardiovascular risk factors² that could affect one of every four Spaniards⁶. The ATP III establishes that a subject has MS when he/she fulfils more than or equal to three of the five following criteria: high blood pressure (or medical treatment for hypertension), impaired fasting glycaemia (or medical treatment for diabetes), hypertriglyceridaemia, low HDL cholesterol levels and abdominal obesity.

Insulin resistance has been linked to MS development⁷. It must be pointed out that there is no scientific consensus as to how to diagnose an insulin-resistance state.

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Nevertheless, for the purposes of this work the HOMA (Homeostasis Model Assessment) model has been chosen. The HOMA is an index that relates fasting insulin and glucose levels⁸. There is no standardised threshold to determine when a subject has insulin resistance. In Spain, Ascaso *et al.*⁹ have established a threshold based on the percentile 90 of fasting insulinaemia and the same percentile of HOMA index, of a control population (subjects without clinical or analytical parameters of insulin resistance).

Early diagnosis of MS and a preventive approach could diminish cardiovascular disease. A healthier lifestyle, with moderate physical activity and adequate nutritional habits, were the initial steps to prevent MS and cardiovascular complications². In spite of its high prevalence and importance, there is no agreement about the dietary factors that may attenuate or promote it.

There is some evidence of the beneficial role of the MD on MS. In a randomised controlled study carried out in Naples (Italy)¹⁰ with 180 MS patients, it was observed that in the intervention group (following a Mediterranean-style diet), the prevalence of MS was reduced by 55.6%, as compared with a reduction of 13.3% in the control group (following a prudent diet) in a 2-year period. In another randomised controlled study carried out in Germany¹¹ with 101 patients with established coronary artery disease, an MD approach could not change metabolic risk factors in a 1-year period. Nevertheless, it must be pointed out that the nutritional intervention developed in the German study was far from being a real MD pattern in some aspects (high intake of red meat and meat products, low use of olive oil, etc.).

The definition of 'MD' is not easy¹². It could be considered as a food pattern that characterises a way of life and a culture, and that could improve health and quality of life of those subjects following it¹³. Some food components of the MD could be: high intake of vegetables, legumes, fruit, nuts and cereal (mostly whole grain); high to moderate intake of fish; low intake of saturated fatty acids but high intake of unsaturated fatty acids (specially olive oil); moderate to low intake of dairy products (specially cheese and yoghurt); low intake of red meat and moderate intake of alcohol (mostly red wine)¹⁴.

In epidemiological studies assessing the relation of the MD and the health parameters, indexes of adherence to a previously established MD food pattern were used¹². The indexes were based on a single score that results from the combination of measured intakes of the different individual components of the MD food pattern.

The present work analysed the relationship between the individual index of adherence to a pre-established MD score, and the prevalence of MS, its criteria and insulin resistance, in a representative sample of a Spanish population.

Material and methods

Subjects

In the Canarian Nutrition Survey (ENCA 1997–1998)¹⁵, a representative sample of the Canarian general population between 6- and 75-year-old was selected by a two-stage stratified sampling method. A total of 1747 individuals participated (67.2% of the original sample). ENCA included two individual questionnaires about diet, lifestyle and health status. Anthropometric variables and blood pressure were also measured. Participants in these home surveys were solicited to have a blood extraction in order to determine biochemical parameters. Seven hundred and eighty-two subjects participated in the biochemical phase (44.8% of the ENCA participants). The present study is based on a sub-sample of 578 adults ≥ 18 years (249 men and 329 women).

The study was approved by the Institutional Committee of Ethics of the Canarian Health Service, and all the study patients gave written informed consent. Details on the methodology have been published elsewhere¹⁶.

Nutritional assessment

The usual food intake in the past 12 months was registered by a semiquantitative Food Frequency Questionnaire (FFQ), including 81 food items. Participants were asked to report how many times and how frequently they consumed these items, selecting one out of five frequency categories (ranging from 'never' to 'daily'). Referred intakes were transformed into grams per day. The FFQ is available online¹⁵. Total energy intake and macronutrient intakes were calculated from the FFQ using the Spanish food composition database developed by Mataix *et al.*¹⁷, complemented with French tables¹⁸. The specific methodology has been published elsewhere¹⁹.

In order to assess the adherence to an MD pattern, a specific score was calculated, based on ten food items. The ten food items were considered as follows:

- (1) Cereal: white bread, whole grain bread, pasta, rice, breakfast sweetened cereals, gofio (roasted wheat or corn flour) and cookies.
- (2) Fruit: apples, avocados, oranges, bananas, papayas, natural fruit juice and jam.
- (3) Vegetables: vegetable soup, lettuce, boiled vegetables, tomatoes, onions and other vegetables.
- (4) Legumes.
- (5) Fish: blue fish, white fish, seafood and octopus.
- (6) Nuts.
- (7) Alcohol from red wine (one glass equivalent to 100 ml of ethanol at 12%).
- (8) Monounsaturated to saturated fatty acids ratio (MUFA/SFA ratio).
- (9) Whole-fat dairy products: whole-fat milk, caramel custard, yoghurt, cream, cheese, margarine and butter.

- (10) Red meat and derivatives: beef, pork, ham, sausages and similar food items, liver and tripe.

Daily intakes of these foods items (in g day^{-1}) were adjusted to 2500 kcal in men and 2000 kcal in women. Then, sex-specific tertiles of the intakes of these ten food items were calculated. Three points were given to the subjects in the third tertile of cereal, fruit, vegetables, fish, nuts and MUFA/SFA ratio; two points to the subjects in the second tertile and one point to the subjects in the first tertile. Whole-fat dairy products and red meat intake received an inverse marking system (three points to the first tertile and one point to the third one). With respect to the alcohol intake from red wine, three points were assigned to moderate consumers (0.1–19.9 and 0.1–39.9 day^{-1} in women and men, respectively) and one point to non-consumers. There were no subjects consuming higher amounts of alcohol from red wine. Finally, the total sum of individual marks in every food item was calculated given the total Mediterranean score (ranging from 10 to 30).

Metabolic Syndrome

The definition of MS used in our work was the one established by the National Cholesterol Education Program's Adult Treatment Panel III (ATP III)². A participant was considered to have MS if three or more of the following criteria were present:

1. Abdominal obesity, defined by waist circumference: Men > 102 cm; Women > 88 cm. Waist circumference was collected with the subject standing, taking as reference half of the distance between the iliac crest and the lowest rib margin. A non-stretch metric measure tape was utilised. There were 2.8% of missing data for this variable.
2. Triglycerides ≥ 150 mg dl^{-1} in serum (missing data = 1.2%).
3. HDL cholesterol < 40 and < 50 mg dl^{-1} for men and women, respectively. All lipid variables were obtained by standardised chemical methods and spectrophotometry (missing data = 1.3%).
4. Blood pressure $\geq 130/85$ mmHg. Blood pressure determination was made in the dominant arm of a seated subject with an automatic tensiometer, separating the first and the second readings by 10 min. The mean of both readings was determined. This criterion was also applied to subjects who were receiving medical treatment with antihypertensive medication (missing data = 2.3%).
5. Fasting glucose ≥ 110 mg dl^{-1} . Subjects had been fasting for 12 h and the glucose was also obtained by standardised chemical methods. This criterion was also applied to subjects who were receiving antidiabetic medication (insulin or oral agents) (missing data = 1.2%).

Insulin resistance

Insulin resistance was considered with two variables: high fasting insulinaemia or high HOMA index. The HOMA index was calculated with the formula = $[(\text{insulin} \times \text{glycaemia})/405]$. Using the methodology described by Ascaso *et al.*⁹, a control population without insulin resistance was used. The control population was selected from those ENCA subjects that fulfil the inclusion criteria (age 30–60 years; absence of family antecedents of diabetes, hypertension or cardiovascular events (acute myocardial infarction/ictus); absence of personal antecedents of diabetes or cardiovascular disease; fasting glycaemia levels < 110 mg dl^{-1} ; blood pressure $< 140/90$ mmHg; absence of antihypertensive medication; triglycerides level < 150 mg dl^{-1} ; body mass index < 25 kg m^{-2} ; waist circumference < 102 cm (men) or < 88 cm (women)). Percentile 90 of fasting insulinaemia in that control population was 14.0195 $\mu\text{U ml}^{-1}$, whereas percentile 90 of HOMA index was 2.8590 UI.

Sociodemographic and lifestyle variables

The variables assessed were: sex, age, educational level (less than elementary, elementary, high school and university), physical activity in free time (sedentary, light, moderate or vigorous), body mass index (BMI, weight in kilogram per height in square metre categorised in < 25 , 25 – 29.9 and ≥ 30 kg m^{-2}), tobacco consumption (smoking, no smoking and ex-smokers), having followed any kind of regimen diet in the past 12 months (yes or no) and total energy intake.

Statistical analysis

The categorical variables were expressed as percentages. Differences between MS and non-MS subjects were evaluated with χ^2 analyses. Continuous variables were expressed as means and standard deviations (SDs) if they followed a normal distribution, or as medians (25th–75th percentiles) in the case of skewed distributions. Differences between MS and non-MS were evaluated with the Student's *t*-test or, if not normally distributed, with the Mann–Whitney *U* test.

A multivariate logistic regression was used to calculate the odds ratios (ORs) for MS prevalence, and for the prevalence of every MS criterion. For these calculations, first tertile of adherence of MD and first tertile of intake of each ten items of the MD index were used as reference category. $P < 0.05$ was considered to be significant. All the statistics were performed with the SPSS software (release 11.0; SPSS Inc., Chicago, IL, USA).

Results

From the total study population, 141 patients (24.4%) met the ATP III definition of MS. The prevalence of every criterion is summarised in Table 1. The most frequent criteria were elevated blood pressure (50.2%), followed by

Table 1 Prevalence of metabolic syndrome, MS criteria and insulin resistance by sex. ENCA Study, *n* = 578

Criteria	Total		Men		Women		<i>P</i>
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
MS	141	24.4	61	24.5	80	24.3	NS
<i>Blood pressure criteria</i>							
SBP \geq 130 and/or DBP \geq 85	284	49.1	157	63.1	127	38.6	0.001
Antihypertensive medication	67	11.6	22	8.8	45	13.7	0.072
Any	295	50.2	161	64.1	134	39.8	0.001
<i>HDL Cholesterol criteria</i>							
HDL $<$ 40 mg dl ⁻¹ (M), $<$ 50 mg dl ⁻¹ (W)	198	34.3	66	26.5	132	40.1	0.001
<i>Triglyceridaemia criteria</i>							
Triglycerides \geq 150 mg dl ⁻¹	149	25.8	79	31.7	70	21.3	0.004
<i>Central obesity criteria</i>							
Waist circ. $>$ 102 cm (M), $>$ 88 cm (W)	201	34.8	76	30.5	125	38.0	0.062
<i>Glycaemia criteria</i>							
Fasting glucose \geq 10 mg dl ⁻¹	61	10.6	30	12.0	31	9.4	NS
Antidiabetic medication ¹	24	4.2	12	4.8	12	3.6	NS
Any	67	11.6	35	14.1	32	9.7	NS
<i>Insulin resistance</i>							
Insulinaemia $>$ 14.02 μ U ml ⁻¹	183	32.3	85	35.1	98	30.2	NS
HOMA index $>$ 2.86 UI	154	27.2	72	29.8	82	25.3	NS

n, number of subjects; NS, non-significant; HDL, high-density lipoprotein cholesterol; M, men; W, women; SBP, systolic blood pressure; DBP, diastolic blood pressure.

¹ Antidiabetic medication, insulin or oral hypoglycemic agents.

central obesity and low HDL cholesterol. Men showed a higher prevalence of hypertriglyceridaemia and elevated blood pressure, while women showed higher prevalence of abdominal obesity and low HDL cholesterol (all differences $P < 0.05$, except for central obesity, $P = 0.06$).

The prevalence of every criterion by age group is shown in Fig. 1. In younger groups, the most prevalent criteria were low HDL cholesterol and hypertension. From 55 years on, more than 80% of the subjects fulfil the elevated blood pressure criterion, and more than 50% fulfil the central obesity criterion.

The insulin-resistance prevalence was 32.3% when high insulinaemic level was used and 27.2% when high HOMA index was used. No relevant differences by sex were detected. The prevalence of insulin resistance increases significantly with age.

In an MD score ranging from 10 to 30 points, the mean score of ENCA subjects was 19.7 points (SD 3.15). The score was higher in men and older subjects, as shown in Fig. 2.

The score was higher in MS subjects [mean score 20.2 (SD 3.2)] than in non-MS subjects [mean score 19.5 (SD 3.1)], $P < 0.05$. In order to consider all the influential variables, a multivariable regression model was developed. Once adjusted, MD adherence was not related to MS prevalence, with an OR (95% CI) of 1.39 (0.75–2.59) for subjects in the second tertile of adherence and an OR 1.37 (0.76–2.46) for subjects in the third tertile of adherence, with respect to the first tertile.

Individual criteria of MS were also considered. Crude analysis showed that the subjects who presented glycaemia criterion (high fasting glycaemia or antidiabetic treatment) showed a higher MD score [mean score 21.0

(SD 2.9)] than the subjects without this criterion [mean score 19.5 (SD 3.1)] $P < 0.05$. Once adjusted (Table 2), the subjects in the third tertile of adherence to the MD pattern (score of adherence ≥ 21) presented a 70% lower prevalence of the blood pressure criterion (P for tendency 0.051) but 2.5 times more prevalence of the glycaemia criterion with respect to the first tertile (score of adherence ≤ 18). The rest of MS criteria and the insulin-resistance prevalence were not significantly associated with the MD score.

The association of the ten food items of the MD pattern with the five MS criteria and insulin-resistance prevalence were considered separately (Table 3).

Red meat intake was associated with a higher prevalence of the blood pressure criterion (elevated blood pressure or antihypertensive treatment), P for tendency 0.028. Moderate alcohol intake from red wine was associated with a lower prevalence of this criterion in women.

With respect to the two dislipemic criteria (high triglyceridaemia and low HDL cholesterol), moderate alcohol intake was associated with a lower prevalence of both criteria, but it was significant only for HDL cholesterol in men. Fruit intake also showed a protective effect on both dislipemic criteria. On the contrary, vegetable intake was associated with a higher prevalence of dislipemia. In both cases, it was significant only in the case of triglyceride criterion.

With respect to the glycaemic homeostasis (glycaemia criterion and insulin-resistance prevalence), cereal intake showed a protective effect, significant in the case of insulin resistance measured by high insulinaemia levels (P for tendency 0.020). Fruit intake showed a relevant

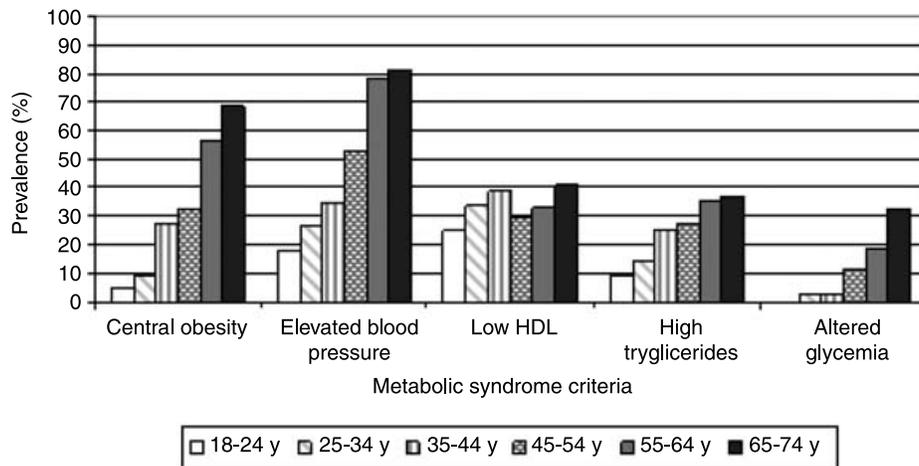


Fig. 1 Prevalence of metabolic syndrome criteria by age group. ENCA Study, $n = 578$

protective effect over high HOMA index. Whole-fat dairy products showed a protective effect on the glycaemia criterion (high fasting glycaemia or antidiabetic treatment), but it showed the reverse effect on insulin resistance, although not significant in later. High mono-unsaturated fatty acid intake (with respect to saturated intake) showed a protective effect on the glycaemia criterion and insulin resistance when measured by the two variables (insulinaemia and HOMA index), P for tendency = 0.06 for both. Finally, moderate intake of alcohol from red wine showed a protective effect on the glycaemic homeostasis, especially in men (not significant).

No noticeable association was observed for the central obesity criterion.

Discussion

One in every four adults presented MS in this representative sample of Spanish population. This prevalence⁶ is one of the highest in the European population-based studies and similar to prevalence described in the USA²⁰. A higher adherence to the MD

was related with a lower prevalence of the blood pressure criterion but a higher prevalence of the glycaemia one.

Subjects with high adherence to the MD index (third tertile, score ≥ 21) showed 70% less prevalence of the blood pressure criterion (elevated blood pressure or antihypertensive treatment) than the subjects with low adherence (first tertile, score ≤ 18), P for tendency 0.051. In the Greek-EPIC cohort²¹, an inverse association between MD adherence and blood pressure has also been described.

The food items involved in the protective effect of the MD on the blood pressure criterion in the ENCA Study were lower red meat intake ($< 40 \text{ g day}^{-1}$) and moderate alcohol intake from red wine ($0.1\text{--}19.9 \text{ g day}^{-1}$ in women). Their protective effects remained even when macro- and micronutrients intake (including proteins, saturated fatty acids, sodium, potassium and alcohol) were included in the model (data not shown).

Recently, a 7-year follow-up study of Japanese–Brazilians aged 40–79 years²² showed that men with the highest tertile of red meat consumption presented a 4.7-fold increase in the risk of developing MS. The red meat

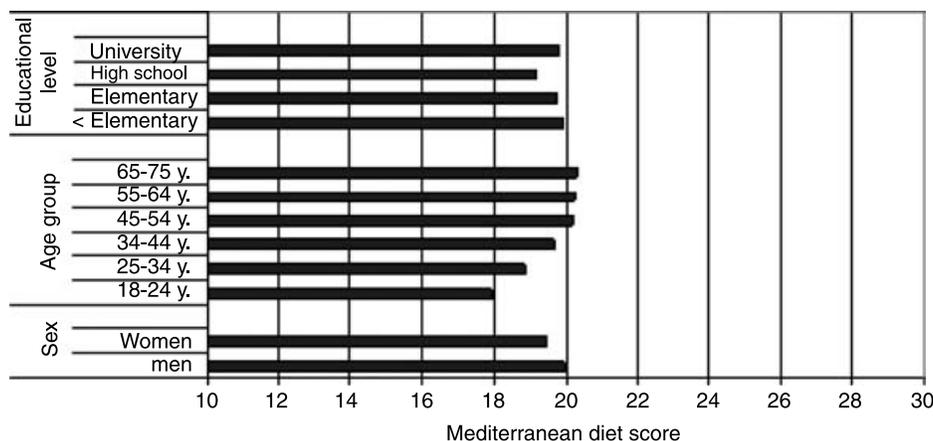


Fig. 2 Mediterranean diet (MD) score, by sex, age group and educational level. ENCA Study, $n = 578$

Table 2 Odds ratio of presence of metabolic syndrome (MS) criteria and insulin resistance, by tertile of adherence to Mediterranean diet (MD). ENCA Study, *n* = 532

Criteria	MD Score	OR ¹ of Criteria	95% CI		<i>P</i>	<i>P</i> tend
			Inf	Sup		
Blood pressure criteria	Tertile 1	1.00				
	Tertile 2	0.88	0.52	1.52		
	Tertile 3	0.58	0.34	0.99	0.045	0.051
HDL Cholesterol criteria	Tertile 1	1.00				
	Tertile 2	0.88	0.55	1.42		
	Tertile 3	0.90	0.56	1.42	NS	NS
Triglyceridaemia criteria	Tertile 1	1.00				
	Tertile 2	1.22	0.72	2.06		
	Tertile 3	1.05	0.63	1.75	NS	NS
Central obesity criteria	Tertile 1	1.00				
	Tertile 2	0.98	0.48	2.02		
	Tertile 3	0.77	0.38	1.56	NS	NS
Glycaemia criteria	Tertile 1	1.00				
	Tertile 2	2.17	0.94	4.99		
	Tertile 3	2.46	1.13	5.37	0.024	0.083
Insulin > 14.02	Tertile 1	1.00				
	Tertile 2	0.76	0.43	1.34		
	Tertile 3	0.67	0.39	1.17	NS	NS
HOMA > 2.86	Tertile 1	1.00				
	Tertile 2	0.89	0.52	1.51		
	Tertile 3	0.94	0.56	1.58	NS	NS

NS, non-significant; *P* tend, *P*-value for tendency test.

¹Adjusted by sex, age, educational level, physical activity level, BMI, tobacco consumption, diet in the past 12 months and energy intake.

effect on blood pressure has extensively been described. In a 7-year follow-up study carried out in 1700 US men, it was observed that those men eating >80 g day⁻¹ of meat showed higher blood pressure levels than men eating <80 g per day²³. In the Oxford-EPIC cohort²⁴ more than 11 000 subjects, aged 20–79 years, were studied, and those who did not refer meat, fish, eggs or dairy products consumption showed 2–4 mmHg less in their mean blood pressure levels than regular meat consumers. In the Nurses's Health Study²⁵, 0.11 mmHg increased in systolic blood pressure was observed for every quintile of increase in meat intake. Similar results were described in the Coronary Artery Risk Development in Young Adults (CARDIA) Study²⁶, while plant food intake (grains, fruit, vegetables, nuts and legumes) was inversely related to elevated blood pressure. In the ENCA Study, vegetables, nuts and legumes intakes were also related with lower prevalence of the blood pressure criterion (no significant).

With respect to the protective effect showed by red wine, the ENCA Study showed that the women who refer moderate alcohol intake (0.1–19.9 g day⁻¹ of alcohol from red wine) presented a two-fold decrease prevalence of the blood pressure criterion with respect to non-consumers. A protective effect of moderate alcohol intake on cardiovascular profile in women has also been described in another Spanish population-based study²⁷.

Nevertheless, it must be highlighted that a deleterious effect of excessive alcohol intake on blood pressure has also been extensively described. Thus, in the National Heart, Lung and Blood Institute Family Heart Study carried

out with a USA adult population group²⁸, a protective effect of 0.1–12 g day⁻¹ of alcohol intake on the blood pressure criterion was described, especially for women. However, when the alcohol intake was >24 g day⁻¹, an incremental risk was described, especially in men.

The food items included in the MD score showed relevant associations with the two dislipemic criteria included in the MS definition (high triglyceridaemia and low HDL cholesterol). Moderate alcohol intake was related to a lower prevalence of low HDL cholesterol, of significance only for men. This effect was maintained when macro- and micronutrients were included in the model, even when total alcohol intake was included [OR 0.56 (95% CI 0.37–0.85)].

The protective effect of alcohol intake on HDL cholesterol has been described in other studies. In the National Heart Study, previously mentioned²⁸ subjects with high alcohol intakes presented a lower prevalence of the HDL criterion than non-alcohol consumers. In the DESIR French study²⁹, alcohol consumption was also associated with higher HDL cholesterol serum levels in both sexes. Similar results were mentioned in a study³⁰ carried out in Brazil. Finally, in the other article of the Spanish population-based study previously mentioned³¹, alcohol consumption showed a positive effect over HDL cholesterol serum levels in men. This protective effect could be partially explained by a direct effect of alcohol on HDL cholesterol synthesis, and by a modification of the activity of the lipoprotein lipase, hepatic lipase and cholesterol-ester transfer protein³¹.

Table 3 Adjusted odds ratio¹ of presence of metabolic syndrome (MS) criteria and insulin resistance, by tertile of intake of the food groups of the Mediterranean diet (MD) pattern. ENCA Study, *n* = 532

	Blood pressure criteria	HDL cholesterol criteria	Triglyceride criteria	Central obesity criteria	Glycaemia criteria	Insulin > 14	HOMA > 3
Cereals T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	1.40 (0.80–2.46)	0.79 (0.50–1.26)	1.37 (0.79–2.37)	0.92 (0.43–1.57)	0.81 (0.36–1.80)	0.53 (0.30–0.96)*	0.66 (0.38–1.13)
T3	1.63 (0.92–2.46)	0.85 (0.54–1.35)	0.89 (0.51–1.57)	1.16 (0.56–2.42)	0.86 (0.39–1.89)	0.52 (0.29–0.94)*	0.70 (0.41–1.21)
Fruit T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.85 (0.48–1.50)	0.69 (0.42–1.13)	0.49 (0.28–0.88)*	0.68 (0.33–1.39)	1.19 (0.50–2.85)	0.63 (0.34–1.18)	0.49 (0.28–0.88)*
T3	1.15 (0.65–2.02)	0.77 (0.47–1.25)	0.69 (0.40–1.18)	0.86 (0.44–1.70)	1.85 (0.82–4.19)	1.30 (0.73–2.32)	0.91 (0.53–1.57)
Vegetables T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.97 (0.55–1.72)	1.31 (0.82–2.08)	1.76 (1.02–3.05)*	1.32 (0.62–2.28)	1.61 (0.66–3.90)	1.36 (0.75–2.46)	1.36 (0.78–2.37)
T3	0.79 (0.42–1.48)	1.17 (0.71–1.92)	1.29 (0.70–2.38)	0.94 (0.46–1.03)	1.60 (0.63–4.06)	0.90 (0.47–1.73)	1.25 (0.68–2.31)
Legumes T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.92 (0.53–1.60)	1.05 (0.66–1.68)	1.30 (0.75–2.25)	0.67 (0.34–1.32)	2.16 (0.92–5.04)	0.66 (0.36–1.19)	0.67 (0.34–1.32)
T3	0.92 (0.53–1.62)	1.36 (0.84–2.19)	1.29 (0.72–2.32)	0.94 (0.46–1.93)	1.82 (0.71–4.68)	1.41 (0.76–2.59)	0.94 (0.46–1.93)
Fish T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.97 (0.56–1.71)	0.79 (0.50–1.26)	0.61 (0.35–1.06)	0.61 (0.29–1.33)	0.57 (0.24–1.36)	1.24 (0.67–2.27)	0.61 (0.29–1.33)
T3	1.13 (0.63–2.03)	0.97 (0.61–1.56)	0.83 (0.47–1.45)	0.50 (0.23–1.10)	1.13 (0.49–2.62)	1.31 (0.71–2.43)	0.50 (0.23–1.10)
Nuts T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.73 (0.41–1.28)	0.77 (0.48–1.23)	1.34 (0.81–2.22)	1.31 (0.62–2.80)	0.70 (0.30–1.65)	0.92 (0.51–1.65)	0.84 (0.48–1.45)
T3	0.83 (0.47–1.46)	0.89 (0.56–1.41)	0.91 (0.53–1.55)	0.88 (0.41–1.90)	1.86 (0.84–4.12)	0.93 (0.51–1.71)	1.23 (0.70–2.14)
Whole-fat dairy T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	1.68 (0.96–2.97)	1.26 (0.80–1.99)	0.62 (0.35–1.09)	1.70 (0.78–3.73)	0.68 (0.31–1.49)	1.48 (0.81–2.69)	1.70 (0.78–3.73)
T3	1.71 (0.94–3.11)	0.90 (0.56–1.44)	0.71 (0.39–1.31)	2.03 (0.89–4.64)	0.27 (0.10–0.75)*	0.98 (0.51–1.89)	2.03 (0.89–4.64)
Red meat T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	1.95 (1.10–3.45)*	0.94 (0.59–1.50)	1.34 (0.81–2.22)	0.69 (0.35–1.40)	0.89 (0.43–1.86)	0.85 (0.48–1.52)	0.69 (0.35–1.40)
T3	2.10 (1.16–3.79)*	1.00 (0.62–1.61)	0.87 (0.51–1.49)	1.01 (0.50–2.07)	0.54 (0.23–1.26)	1.07 (0.59–1.95)	1.01 (0.50–2.07)
Mufa/sfa ratio T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2	0.77 (0.44–1.35)	0.81 (0.52–1.31)	0.85 (0.50–1.43)	1.14 (0.53–2.49)	0.52 (0.23–1.19)	0.55 (0.30–0.99)*	0.63 (0.36–1.09)
T3	0.79 (0.43–1.46)	0.93 (0.59–1.48)	1.28 (0.77–2.11)	1.09 (0.48–2.52)	0.44 (0.19–1.02)	0.53 (0.28–1.01)	0.49 (0.27–0.89)*
Red wine alcohol T1 (ref)	1.00	1.00	1.00	1.00	1.00	1.00	1.00
T2 (men)	1.13 (0.77–1.69)	0.49 (0.33–0.73)**	0.83 (0.45–1.55)	1.06 (0.43–2.65)	0.58 (0.33–1.01)	0.81 (0.56–1.18)	0.90 (0.63–1.29)
T2 (women)	0.46 (0.29–0.74)**	0.85 (0.46–1.56)	0.96 (0.62–1.49)	0.84 (0.47–1.51)	1.56 (0.82–2.98)	0.85 (0.53–1.36)	0.82 (0.54–1.26)

T1, first tertile; T2, second tertile; T3, third tertile; NA, not applicable (only two groups); MUFA/SFA, monounsaturated to saturated fatty acids ratio.

¹Adjusted by sex (except red wine alcohol intake), age, educational level, physical activity level, BMI, tobacco consumption, diet in the past 12 months, energy intake and intake of rest of food groups included in the MD score. **P* < 0.05; ***P* < 0.01.

Fruit intake also showed a protective effect on both dyslipemic criteria. Moderate fruit intake (mean intake 375 g day^{-1}) was associated with a twofold decrease in triglyceride criterion prevalence with respect to low fruit intake ($< 250 \text{ g day}^{-1}$), whereas high fruit intake ($> 450 \text{ g day}^{-1}$) showed no significant association. The protective effect of moderate fruit intake remained even when macro- and micronutrients were included in the model (1.85-fold decrease for the second tertile of fruit intake). In the Baltimore Longitudinal Study of Ageing³², subjects with a 'healthier' food pattern, where 10% of their energy was provided by fruit, presented 16% lower triglyceride serum levels than subjects whose fruit-energy intake was $< 5\%$. Some randomised controlled studies³³ have shown that fruit supplementation for one month decreases triglycerides levels by 12% in a high risk population (hypercholesterolaemic patients after coronary bypass surgery), and lower levels of total cholesterol and LDL cholesterol were also observed. In the ENCA Study, fruit intake showed a protective effect on low HDL cholesterol levels (Table 3), and also on high LDL cholesterol level ($\text{LDL} \geq 130 \text{ mg dl}^{-1}$), with and OR 0.59 (95% CI 0.35–0.98) for the second tertile and 0.53 (95% CI 0.32–0.90) for the third tertile, with respect to the first fruit intake tertile (all $P < 0.05$).

With respect to the vegetable intake, an unexpected higher prevalence of the triglyceridaemia criterion was observed in subjects referring medium intakes of vegetables (mean vegetable intake 400 g day^{-1}) with respect to the lowest intake ($< 200 \text{ g day}^{-1}$), even when macro- and micronutrients intake were considered. Once again, the highest tertile showed no relevant association. In the Framingham Offspring Cohort Study³⁴, fibre intake from vegetables was associated with higher (although non-significant) risks of developing MS (OR 1.15). The association observed in the ENCA Study could be due to the cross-sectional design of the study, and subjects with diagnosed hypertriglyceridaemia could be following a healthier diet with increased intakes of vegetables. Nevertheless, the exclusion of subjects that refer being on a diet in the past 12 months did not materially change the results, with an OR of present triglyceridaemia criterion of 1.84 (95% CI 0.99–3.41) for the second tertile and 1.42 (95% CI 0.70–2.87) for the third tertile, with respect to the first tertile. Those results should be assessed in larger prospective studies.

Finally, the MD influence on glucose homeostasis was assessed. As Table 2 shows, the subjects in the highest tertile of MS adherence presented a 2.5-fold increase in glycaemic criteria (high fasting glycaemia or antidiabetic treatment), although no worth-mentioning effect was seen on the insulin-resistance criterion. Subjects with higher intakes of whole-fat dairy products (third tertile, mean intake 600 g day^{-1}) showed a 3.7-fold decreased prevalence of the glycaemic criterion with respect to subjects with lower intakes (first tertile, intakes $< 140 \text{ g day}^{-1}$). The

results remained even when macro- and micronutrients intakes were considered. An opposite effect was seen on the insulin-resistance criterion (not relevant).

With respect to the glycaemia criterion, these results must be taken with caution, because the protective effect of whole-fat dairy products could also be due to the cross-sectional design of the study. Most subjects that fulfil glycaemic criteria were previously known to be diabetic patients. Most of them were following a diet, and they have probably received nutritional counselling regarding a healthier diet (including low whole-fat dairy products intake). Nevertheless, high intake of whole-fat dairy products has been associated with lower weight gain³⁵, and this factor would decrease the risk of developing diabetes. In the Women's Health Study carried out in the USA³⁶, dairy products intake was associated with lower prevalence of MS, and the protective effect was stronger for whole-fat dairy products (P for tendency 0.002) than for low-fat dairy products (P for tendency 0.07). Those results should be assessed in larger prospective studies.

Higher cereal intake was related with a lower prevalence of the glycaemic criterion and the insulin-resistance criterion. The subjects referring cereal intake $> 150 \text{ g day}^{-1}$ presented half the risk of hyperinsulinaemia than subjects with lower intakes. Moderate fruit intake (mean intake 375 g day^{-1}) was associated with a twofold decrease in high HOMA index prevalence. It was also associated with lower hyperinsulinaemia prevalence, although not significantly. The results remained even when macro- and micronutrients intakes were considered (OR 0.53 for the second tertile and 0.56 for the third tertile).

There are numerous studies analysing the relationship between carbohydrate intake and glucose homeostasis. With a similar methodology as the one used for the ENCA (cross-sectional population-based study), the Framingham Offspring Cohort Study³⁴ showed that whole-grain cereals' and fibre intakes (especially, fibre from cereal and fibre from fruit) were associated with a lower mean HOMA index. In the Insulin Resistance Atherosclerosis Study (IRAS)³⁷, whole-grain intake was associated with higher insulin sensitivity and lower insulin levels. In the Inter99 Study³⁸, every 100 g day^{-1} of increase in fruit and vegetable intake was related with a 0.99 UI decrease in HOMA index, the same decrease that was described for every 1% of energy provided by fructose (fruit sugar with low glycaemic index).

One possible pathophysiology explanation could be that whole-grain cereals' intake and low glycaemic index foods result in a significant decrease in the after-meal insulin response. This effect could be partially explained by the nutrient composition of those foods (fibre content), which results in a lower rate of gastric emptying and an increase satiation³⁹.

Other components of cereals and fruit (like magnesium and vitamin E) have also been involved³⁷. The IRAS

authors mentioned that the inclusion of fibre and magnesium in their model attenuated the relationship between cereal intake and insulin sensitivity. Nevertheless, in the ENCA Study, the inclusion of these nutrients did not materially affect the described association.

The other food item that was related with glucose homeostasis was the monounsaturated to saturated fatty acids ratio. The subjects that refer intakes of MUFA higher than SFA (MUFA/SFA ratio > 1) showed a lower prevalence of elevated HOMA index, and a lower prevalence of hyperinsulinaemia. This protective role persists even when macro- and micronutrients were considered (OR for the second and the third tertiles 0.57 and 0.36 for HOMA and 0.49 and 0.41 for hyperinsulinaemia, respectively, compared with the first tertile). In an interesting review on carbohydrates and fats' effects on insulin resistance⁴⁰, it was remarked that the substitution of a high SFA diet (MUFA/SFA ratio 0.74) for a high MUFA diet (MUFA/SFA ratio 2.21) was related with a 10% increase in insulin sensitivity. Olive oil is one of the main MUFA sources in the ENCA subjects, being consumed by 80% of the population⁴¹.

In a Spanish study, the prevalence of insulin resistance was 50% lower in subjects that cooked with olive oil, compared with those that used other vegetable oils (sunflower seed or mixed)⁴². It has been mentioned that SFA worsens insulin resistance, whereas MUFA and PUFA improve it, due to a modification in the lipid composition of cell membranes in liver and muscle tissues, where the oleic acid concentration is high⁴³. Other possible effects could be the regulation of gene expression related to insulin sensitivity⁴³.

In conclusion, following a diet approaching the MD model, especially with low intake of red meat, moderate alcohol consumption and high intakes of fruit, cereals and monounsaturated fatty acids, has been related with a lower prevalence of MS criteria and insulin resistance in the general population.

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