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Original Contribution

The Mediterranean Diet and Incidence of Hypertension

The Seguimiento Universidad de Navarra (SUN) Study

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The Mediterranean diet is receiving increasing attention in cardiovascular epidemiology. The association of adherence to the Mediterranean diet with the incidence of hypertension was evaluated among 9,408 men and women enrolled in a dynamic Spanish prospective cohort study during 1999–2005. Dietary intake was assessed at baseline with a validated semiquantitative food frequency questionnaire, and a 9-point Mediterranean diet score was constructed. During a median follow-up period of 4.2 years (range, 1.9–7.9), 501 incident cases of hypertension were identified. After adjustment for major hypertension risk factors and nutritional covariates, adherence to the Mediterranean diet was not associated with hypertension (the hazard ratio was 1.10 (95% confidence interval (CI): 0.81, 1.41) for moderate adherence and 1.12 (95% CI: 0.79, 1.60) for high adherence). However, it was associated with reduced changes in mean levels of systolic blood pressure (moderate adherence, −2.4 mm Hg (95% CI: −4.0, −0.8); high adherence, −3.1 mm Hg (95% CI: −5.4, −0.8)) and diastolic blood pressure (moderate adherence, −1.3 mm Hg (95% CI: −2.5, −0.1); high adherence, −1.9 mm Hg (95% CI: −3.6, −0.1)) after 6 years of follow-up. These results suggest that adhering to a Mediterranean-type diet could contribute to the prevention of age-related changes in blood pressure.

blood pressure; dairy products; diet; diet, Mediterranean; food; hypertension; longitudinal studies

Abbreviations: CI, confidence interval; DASH, Dietary Approaches to Stop Hypertension; MUFA, monounsaturated fatty acid(s); PREDIMED, Prevención con Dieta Mediterránea; PUFA, polyunsaturated fatty acid(s); SFA, saturated fatty acid(s); SUN, Seguimiento Universidad de Navarra.

Hypertension is an important cause of disability and mortality throughout the world. Worldwide, approximately 7.6 million deaths (13.5% of all deaths) and 92 million disability-adjusted life years (6.0% of all disability-adjusted life years) are attributable to high blood pressure (1). One of the basic strategies for addressing this public health problem involves a population-wide approach to prevent the rise in blood pressure with age and to achieve primary prevention by improving dietary and lifestyle habits (2). Therefore, it is crucial to identify dietary patterns that have a preventive effect on the development of hypertension.

Greater adherence to a Mediterranean food pattern has been shown to be associated with substantial reductions in total mortality and cancer and cardiovascular disease mortality (3, 4). The Mediterranean diet has been described by the following characteristics: an abundance of plant foods (fruits, vegetables, breads, other forms of cereals, potatoes, beans, nuts, and seeds); minimally processed, seasonally fresh, and locally grown foods; fresh fruit as the typical daily dessert, with sweets containing concentrated sugars or honey consumed only a few times per week; olive oil as the main source of fat; dairy products (principally cheese and yogurt) only in low-to-moderate amounts; red meat in low amounts; and wine, usually red wine, in low-to-moderate amounts, normally with meals (5). The beneficial effects of this food pattern or some of its constituents on

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cardiovascular disease risk factors and on the incidence of high blood pressure have been previously reported using operational definitions (6–8). Additionally, links between adherence to the Mediterranean diet and reduced incidence of the metabolic syndrome (9) and diabetes mellitus (10) have recently been observed. However, to our knowledge, there is no evidence from either large prospective cohort studies or long-term clinical trials regarding the overall effect of the Mediterranean food pattern on the risk of hypertension.

The Seguimiento Universidad de Navarra (SUN) Study, a prospective Mediterranean cohort study conducted in Spain, provides an excellent opportunity to evaluate the role of the Mediterranean food pattern in the development of hypertension. Therefore, we prospectively examined the association between adherence to a Mediterranean food pattern and the incidence of hypertension using a 9-point Mediterranean diet score (3, 9, 10) in the SUN Study cohort.

MATERIALS AND METHODS

Study cohort

The SUN Study is a dynamic Spanish prospective cohort study with permanently open recruitment. Participants are all university graduates, nurses, and other educated adults who are contacted and followed up using mailed questionnaires. The study methods have been described in detail previously (10, 11). In brief, beginning in December 1999, all graduates of the University of Navarra, other university graduates and educated professionals, and registered nurses in several Spanish provinces received a mailed questionnaire and a letter of invitation to participate in the SUN Study. Response to the initial questionnaire was considered informed consent to participate in the study. The project protocol was approved by the institutional review board of the University of Navarra.

After the baseline assessment, participants received biennial mailed follow-up questionnaires collecting a wide variety of information about diet, lifestyle, risk factors, and medical conditions. Up to 5 additional mailings were sent to nonrespondents.

As of February 2008, the SUN Study had enrolled 19,057 participants aged 20–90 years at baseline. Among them, 15,552 persons were recruited before May 2005 and therefore were able to receive and answer the first follow-up questionnaire. There were 9,190 participants who completed the 2-year follow-up questionnaire, 6,428 who completed the 4-year follow-up questionnaire, and 3,509 who completed the 6-year follow-up questionnaire.

We excluded 1,733 participants who had hypertension at baseline; 1,536 who reported a baseline history of cardiovascular disease, cancer, or diabetes; and 1,349 who had missing values for any covariate. We also excluded female participants whose total energy intake was less than 500 kcal/day or greater than 3,500 kcal/day and male participants whose total energy intake was less than 800 kcal/day or greater than 4,000 kcal/day (1,563 persons excluded). After application of the exclusion criteria, 10,629 participants were available for follow-up; among them, 9,408 (89%) responded to at least 1 follow-up questionnaire and were included in the final analysis.

Baseline data collection

Dietary habits at baseline were assessed using a semiquantitative food frequency questionnaire with 136 items, previously validated in Spain (12). The questionnaire was based on typical portion sizes and had 9 options for the frequency of intake of each food item (ranging from never or almost never to 6 or more times per day) during the previous year. Trained dieticians updated the nutrient database using the latest available information included in the food composition tables for Spain (13, 14).

The baseline questionnaire requested information about a large array of sociodemographic factors (sex, age, university degree, marital status, and employment status), anthropometric measures (weight, height), health-related habits (smoking status, physical activity), and clinical variables (use of medication, personal and family history of hypertension, coronary heart disease, cancer, and other diseases). Body mass index was defined as weight in kilograms divided by the square of height in meters. The questionnaire assessed involvement in 17 different activities and amounts of time spent in them. We assigned a multiple of the resting metabolic rate (metabolic equivalent score) to each of these activities using previously published guidelines (15) in order to quantify the average intensity of physical activity. The validity of data on self-reported weight, body mass index, and self-reported leisure-time physical activity in the SUN cohort has been previously reported (16, 17).

Mediterranean diet scale

We used the score proposed by Trichopoulou et al. (3) to estimate the degree of adherence to the traditional Mediterranean dietary pattern. This score includes 9 components: vegetables, legumes, fruits and nuts, cereals, fish, meat and meat products, dairy products, alcohol, and the ratio of monounsaturated fatty acids (MUFA) to saturated fatty acids (SFA). Values of 0 or 1 were assigned to each of the 9 components, using as cutoffs the sex-specific median values for the cohort participants for all components except alcohol. Thus, for 5 beneficial components (vegetables, legumes, fruits and nuts, cereals, and fish), subjects whose consumption was at or above the sex-specific median were assigned a value of 1, while those whose consumption was below the median were assigned a value of 0. For components presumed to be detrimental (meats or meat products and dairy products), participants whose consumption was below the sex-specific median were assigned a value of 1 and participants whose consumption was at or above the median were assigned a value of 0. For alcohol intake, a value of 1 was assigned to men who consumed 10–50 g/day and women who consumed 5–25 g/day. Finally, the ratio of MUFA to SFA was used to assess the quality of fat intake, giving a value of 0 to participants whose MUFA:SFA ratio was below the sex-specific median and a value of 1 to participants whose ratio was at or above the median.

If participants had all of the characteristics of the Mediterranean diet, their score was the highest possible (9 points), reflecting maximum adherence. If they had none of the characteristics, their score was the minimum possible (0 points), reflecting no adherence at all. Adherence to the Mediterranean diet was categorized as low (score 0–2), moderate (score 3–6), or high (score 7–9) (10).

Ascertainment of hypertension

The study endpoint was incident hypertension diagnosed between the dates of completion of the baseline questionnaire and the last follow-up questionnaire. Participants were asked about receipt of a medical diagnosis of hypertension in the baseline and follow-up questionnaires, as well as the date of diagnosis. The baseline questionnaire and the third (6-year) follow-up questionnaire also asked for information regarding participants' most recent systolic and diastolic blood pressure values. Finally, the follow-up questionnaires inquired as to whether participants had had their blood pressure measured in the time elapsed since the previous questionnaire.

Participants were considered to have hypertension at baseline if they reported a medical diagnosis of hypertension, a systolic blood pressure greater than or equal to 140 mm Hg, a diastolic blood pressure greater than or equal to 90 mm Hg, or use of antihypertensive medication (18). Incident cases of hypertension were defined as participant-reported receipt of a physician's diagnosis of hypertension on the follow-up questionnaire and no hypertension at baseline. The diagnosis of hypertension in this cohort has been validated in a previous study (19). Among participants reporting a diagnosis of hypertension, 82.3% (95% confidence interval (CI): 72.8, 92.8) of cases were confirmed in a domiciliary visit at which the participant's blood pressure was measured twice (using a standardized protocol) by a physician blinded to the self-reported questionnaire information (19). Among participants who did not report a diagnosis of hypertension, 85.4% (95% CI: 72.4, 89.1) were confirmed to be nonhypertensive during the domiciliary visit (19).

Statistical analysis

For each participant, person-time of follow-up was calculated from the date of completion of the baseline questionnaire to the date of diagnosis of hypertension or the date of completion of the last follow-up questionnaire, whichever occurred first. We estimated hazard ratios for hypertension and their 95% confidence intervals across increasing categories of adherence to the Mediterranean diet using Cox proportional hazards models, controlling for the following variables: age, sex, baseline body mass index, family history of hypertension, hypercholesterolemia, caffeine intake, sodium intake, total energy intake, physical activity, and smoking. In all analyses, the lowest adherence category (Mediterranean diet adherence score of 0–2) was considered the reference category. Statistical interaction was assessed by means of likelihood ratio tests in which full models, including interaction terms, were compared with reduced models without interaction terms.

We also quantified the relation of Mediterranean diet adherence to relative average change in blood pressure among participants without hypertension who had completed the 6-year follow-up assessment, using multiple linear regression models with adjustment for age, sex, body mass index, family history of hypertension, hypercholesterolemia, basal blood pressure, caffeine intake, total energy intake, physical activity, and smoking. The reference category was the lowest level of adherence to the Mediterranean diet, and we estimated differences in blood pressure changes with respect to that category.

We conducted linear trend tests across increasing categories of Mediterranean diet adherence by treating the Mediterranean diet score (range, 0–9) as a continuous variable.

All P values are 2-tailed, and statistical significance was set a priori at $P < 0.05$. For all analyses, we used SPSS, version 15.0 (SPSS, Inc., Chicago, Illinois).

RESULTS

Baseline characteristics

The median duration of follow-up was 4.2 years (range, 1.9–7.9). During 41,126 person-years of follow-up, 501 incident cases of hypertension were identified. Baseline characteristics of the study population according to sex and category of adherence to the Mediterranean diet are presented in Table 1.

Men had a higher mean age, a higher body mass index, a greater level of physical activity, and a higher alcohol intake. Mean fruit consumption, mean vegetable consumption, intake of low-fat dairy products, and intake of olive oil were higher among women. Participants with better adherence to the Mediterranean diet were older, more physically active, and less likely to be current smokers.

Mediterranean diet adherence and risk of hypertension

We evaluated the association between baseline adherence to the Mediterranean diet and risk of incident hypertension (Table 2). In the multivariate-adjusted analysis, increased adherence to the traditional Mediterranean diet was not associated with the development of hypertension. Compared with those with the lowest adherence to the Mediterranean food pattern (score 0–2), the hazard ratio for hypertension among participants with moderate adherence to the Mediterranean food pattern (score 3–6) was 1.10 (95% CI: 0.81, 1.41). The hazard ratio for those with the highest adherence (score 7–9) was 1.12 (95% CI: 0.79, 1.60). We conducted this analysis after excluding participants with very low or very high total energy intakes, using the criteria suggested by Willett (total energy intakes of <500 kcal/day or >3,500 kcal/day for women and <800 kcal/day or >4,000 kcal/day for men) (20). When we repeated this analysis without excluding any participants because of high or low values for total energy intake, no appreciable change was observed, and the estimates were attenuated only slightly (data not shown).

When we specifically assessed the association with hypertension risk for each of the 9 components of the

Table 1. Baseline Characteristics of the Study Population (n = 9,408), by Sex and Level of Adherence to the Mediterranean Diet, Seguimiento Universidad de Navarra (SUN) Study, Spain, 1999–2005[a]

	Women (n = 5,825)	Men (n = 3,583)	Adherence to the Mediterranean Diet: Low (Score 0–2) (n = 1,535)	Moderate (Score 3–6) (n = 6,730)	High (Score 7–9) (n = 1,143)
Sociodemographic and lifestyle factors					
Age, years	34.0 (9.7)	39.4 (11.2)	32 (9)	36 (10)	41 (12)
Body mass index[b]	22 (3)	25 (3)	23 (3)	23 (3)	24 (3)
Physical activity, metabolic equivalent-hours/week	22 (18)	29 (26)	21 (19)	25 (22)	28 (24)
Hypercholesterolemia, %	11	19	9	13	24
Family history of hypertension, %	49	47	46	48	51
Alcohol intake, g/day	4 (6)	10 (12)	4 (7)	6 (10)	9 (9)
Current smoker, %	25	21	24	24	20
Mineral intake					
Sodium, g/day	3.1 (1.9)	3.7 (2.4)	3.6 (2.4)	3.3 (2.1)	3.2 (1.9)
Potassium, g/day	4.8 (1.5)	4.6 (1.5)	3.8 (1.0)	4.7 (1.5)	5.8 (1.6)
Calcium, g/day	1.3 (0.5)	1.2 (0.4)	1.2 (0.4)	1.2 (0.4)	1.3 (0.4)
Magnesium, mg/day	411 (118)	409 (118)	338 (84)	412 (113)	501 (121)
Dietary consumption, servings/day					
Fruits	2.5 (2.0)	2.0 (1.8)	1.2 (0.9)	2.3 (1.9)	3.5 (2.3)
Vegetables	2.4 (1.4)	1.9 (1.3)	1.4 (0.8)	2.2 (1.4)	3.1 (1.5)
Legumes	0.4 (0.3)	0.4 (0.3)	0.3 (0.3)	0.4 (0.3)	0.5 (0.3)
Nuts and dried fruits	0.2 (0.3)	0.2 (0.3)	0.1 (0.1)	0.2 (0.3)	0.3 (0.4)
Cereals	1.8 (1.2)	2.1 (1.4)	1.4 (1.1)	1.9 (1.3)	2.5 (1.4)
Meat	1.8 (0.8)	2.0 (0.9)	2.2 (0.9)	1.9 (0.9)	1.5 (0.7)
Fish	0.7 (0.4)	0.7 (0.4)	0.5 (0.3)	0.7 (0.4)	1.0 (0.4)
Eggs	0.4 (0.2)	0.4 (0.3)	0.4 (0.3)	0.4 (0.3)	0.4 (0.2)
Dairy products	3.2 (1.7)	2.8 (1.6)	2.4 (1.4)	1.7 (1.3)	1.0 (0.8)
Low-fat dairy products	1.5 (1.5)	0.9 (1.2)	0.8 (1.2)	1.3 (1.4)	1.7 (1.5)
Intake of other dietary constituents					
Olive oil, g/day	20 (16)	17 (14)	13 (12)	19 (15)	24 (16)
Fiber, g/day	27 (12)	26 (11)	18 (6)	27 (11)	37 (13)
Fiber from cereal, g/day	3.3 (2.9)	3.4 (2.9)	2.4 (1.9)	3.3 (2.8)	5.0 (3.9)
Caffeine, mg/day	45 (39)	46 (41)	43 (40)	46 (40)	45 (37)
Energy intake					
Total energy intake, kcal/day	2,319 (567)	2,488 (652)	2,261 (580)	2,387 (615)	2,528 (548)
Percentage of energy intake					
Carbohydrates	43 (7)	43 (7)	41 (7)	43 (7)	47 (7)
Protein	18 (3)	18 (3)	18 (3)	18 (3)	18 (3)
Vegetable protein	5.3 (1.2)	5.2 (1.2)	4.4 (0.9)	5.3 (1.1)	6.4 (1.2)
Lipids	37 (7)	36 (6)	40 (6)	37 (6)	33 (6)
Saturated fatty acids	13 (3)	13 (3)	15 (3)	13 (3)	10 (2)
Monounsaturated fatty acids	16 (4)	15 (3)	16 (3)	16 (4)	15 (4)
Polyunsaturated fatty acids	5.3 (1.7)	5.3 (1.5)	5.5 (1.7)	5.3 (1.6)	5.1 (1.5)

[a] Values are expressed as mean (standard deviation) unless otherwise stated.
[b] Weight (kg)/height^2 (m^2).

Mediterranean food pattern score, we found a direct association with intermediate alcohol intake (hazard ratio = 1.25, 95% CI: 1.03, 1.51) but an inverse association for consumption of legumes above the sex-specific median level (hazard ratio = 0.84, 95% CI: 0.70, 1.00) after adjusting for age, sex, body mass index, family history of hypertension,

Table 2. Hazard Ratios for Hypertension According to Level of Adherence to the Mediterranean Diet, Seguimiento Universidad de Navarra (SUN) Study, Spain, 1999–2008

Adherence to Mediterranean Diet	No. of Participants	No. of Incident Cases	Person-Years of Follow-up	Age- and Sex-Adjusted		Multivariate-Adjusted[a]	
				HR	95% CI	HR	95% CI
Low (score 0–2)[b]	1,535	62	7,041	1.00		1.00	
Moderate (score 3–6)	6,730	359	29,436	1.11	0.85, 1.46	1.10	0.81, 1.41
High (score 7–9)	1,143	80	4,649	1.17	0.83, 1.64	1.12	0.79, 1.60
P for trend				0.46		0.41	

Abbreviations: CI, confidence interval; HR, hazard ratio.
[a] Adjusted for age, sex, body mass index, family history of hypertension, hypercholesterolemia, caffeine intake, sodium intake, total energy intake, physical activity, and smoking.
[b] Reference category.

hypercholesterolemia, caffeine intake, total energy intake, physical activity, smoking, and the other components of the Mediterranean diet score. No significant association was apparent for any of the other 7 components.

When we assessed the role of intake of MUFA or polyunsaturated fatty acids (PUFA), we found that persons with higher levels of MUFA intake had a lower risk of hypertension; however, the results were not statistically significant (for the fifth quintile vs. the first quintile, multivariate-adjusted hazard ratio = 0.81, 95% CI: 0.59, 1.11; *P* for trend = 0.10). We did not observe any significant association between PUFA intake and the risk of hypertension (data not shown).

We did not observe any significant interaction between Mediterranean diet adherence and age, sex, or body mass index.

Mediterranean diet adherence and blood pressure change

We also assessed the association between average difference in the change in blood pressure from baseline to 6-year follow-up and Mediterranean diet adherence score among participants without hypertension who had completed the 6-year follow-up assessment. Of 2,990 participants who answered the 6-year questionnaire and did not have incident hypertension, 1,513 provided blood pressure values at baseline and 6 years later. A significant inverse association between adherence to the Mediterranean diet and blood pressure change was apparent (Table 3). All categories of adherence to the Mediterranean diet showed lower levels of systolic and diastolic blood pressure change than the category with low adherence. Adjusted relative differences in

Table 3. Association Between Adherence to the Mediterranean Diet and Average Difference in Blood Pressure Change[a] (mm Hg) Among Nonhypertensive Participants Who Completed the 6-Year Follow-up Assessment (n = 1,513), Seguimiento Universidad de Navarra (SUN) Study, Spain, 1999–2008

	Adherence to the Mediterranean Diet						*P* for Trend
	Low (Score 0–2)[b] (n = 229)		Moderate (Score 3–6) (n = 1,109)		High (Score 7–9) (n = 175)		
	Change	95% CI	Change	95% CI	Change	95% CI	
Systolic blood pressure, mm Hg							
Absolute change	1.3		0		−0.5		
Relative change							
Age- and sex-adjusted	0	Referent	−1.9	−3.7, −0.1	−3.2	−5.7, −0.7	0.02
Multivariate-adjusted[c]	0	Referent	−2.4	−4.0, −0.8	−3.1	−5.4, −0.8	0.01
Diastolic blood pressure, mm Hg							
Absolute change	0		0.1		0.2		
Relative change							
Age- and sex-adjusted	0	Referent	−0.5	−1.9, 0.9	−1.0	−3.0, 1.0	0.18
Multivariate-adjusted[c]	0	Referent	−1.3	−2.5, −0.1	−1.9	−3.6, −0.1	0.05

Abbreviation: CI, confidence interval.
[a] Blood pressure after 6 years of follow-up minus blood pressure at baseline.
[b] Reference category.
[c] Adjusted for age, sex, body mass index, family history of hypertension, hypercholesterolemia, basal blood pressure, caffeine intake, total energy intake, physical activity, and smoking.

systolic blood pressure were −2.4 mm Hg (95% CI: −4.0, −0.8) for persons with intermediate adherence (score 3–6) and −3.1 mm Hg (95% CI: −5.4, −0.8) for persons with high adherence (score 7–9) (*P* for trend = 0.01). The relative differences for diastolic blood pressure change were −1.3 mm Hg (95% CI: −2.5, −0.1) for moderate adherence and −1.9 mm Hg (95% CI: −3.6, −0.1) for high adherence (*P* for trend = 0.05). When we did not exclude persons with more than 6 years of follow-up who had developed hypertension during the follow-up period (n = 267), the results were very similar, also showing a monotonic significant inverse trend of blood pressure change with increasing adherence to the Mediterranean diet (test for trend: $P = 0.04$ and $P = 0.02$ for systolic and diastolic blood pressure, respectively) (data not shown).

DISCUSSION

In this prospective Spanish cohort study, which included more than 41,000 person-years of follow-up, adherence to the traditional Mediterranean diet was not associated with the risk of hypertension. Adherence to this food pattern, however, appeared to be inversely associated with changes in average systolic and diastolic blood pressure levels over time among participants who had completed the 6-year follow-up assessment and were not hypertensive at baseline.

Our study had certain limitations. First, dietary exposures can be misclassified despite the good correlation between food frequency questionnaires and usual diet (21). Even though the validation study of our dietary questionnaire demonstrated fair validity and reliability (12), misclassification of dietary exposures could have occurred. Another important limitation is the fact that hypertension status was self-reported. However, the validity of a self-reported medical diagnosis of hypertension in this highly educated cohort has been sufficiently demonstrated elsewhere (19).

Among participants with 6 years of follow-up (n = 3,509), the proportion who provided their blood pressure levels (n = 2,685) was only 77%. However, no significant differences in mean baseline levels of physical activity or alcohol consumption were observed between persons who provided data on their blood pressure and those with missing data. Women, older participants, and those with a higher body mass index were more likely to provide data about their blood pressure after the 6-year follow-up, but we adjusted all of the estimates for these variables.

Substantial evidence has accrued linking adherence to the Mediterranean food pattern to a reduced risk of total mortality and the incidence of cardiovascular disease (3, 4, 22). Thus, we considered the possibility that the reduction in the risk of hypertension could be one of the main pathways that might explain this beneficial effect of the Mediterranean diet on cardiovascular clinical outcomes.

The Dietary Approaches to Stop Hypertension (DASH) Trial, which included 459 adults aged 22 years or older, tested 3 diets for 8 weeks. DASH investigators found preventive effects for a diet rich in fruits and vegetables—especially a combination diet rich in fruits, vegetables, and low-fat dairy products—and for reduced intakes of saturated fat and total fat. Among the 326 participants without hypertension in the DASH Trial, the combination diet reduced systolic and diastolic blood pressures by 3.5 mm Hg and 2.1 mm Hg more, respectively, than the control diet. However, the DASH Trial and other trials that assessed the effects of dietary interventions on blood pressure (23–26) were not designed to evaluate the long-term effect of diet on blood pressure (27).

In the Prevención con Dieta Mediterránea (PREDIMED) Study, Estruch et al. (7) evaluated the effect of the Mediterranean diet on the risk of cardiovascular disease in 772 men and women aged 55–80 years at high risk of cardiovascular disease and reported decreased systolic and diastolic blood pressures after 3 months of follow-up in the 2 Mediterranean diet groups compared with participants assigned to a low-fat diet group. Our results agreed with those of the PREDIMED Study when we examined the association between Mediterranean diet adherence and average difference in blood pressure change among participants without hypertension who had completed the 6-year follow-up questionnaire. Nevertheless, the short-term nature of the PREDIMED trial is a limitation that could weaken the conclusions.

We did not repeat the full-length food frequency questionnaire to assess dietary changes during the follow-up of participants, and we used only baseline food habits as the relevant exposure. Therefore, we do not know whether dietary changes that may have occurred during the course of the study may have concealed some potentially protective effect afforded by a Mediterranean food pattern.

In addition, there could be other reasons for the lack of association between greater adherence to the Mediterranean diet and the development of hypertension found in our study. On the one hand, observed absolute differences in food habits between low- and high-adherence subjects in our cohort were not very large. Therefore, this between-subject homogeneity in exposure could partly explain our null findings. On the other hand, by using the Mediterranean diet score proposed by Trichopoulou et al. (3), we were indirectly assuming that intermediate levels of total alcohol consumption (5–25 g/day among women or 10–50 g/day among men) might be protective against hypertension. Nevertheless, a direct association between total alcohol consumption and hypertension is very likely, because interventions aimed at reducing total alcohol consumption have obtained clinically significant reductions in blood pressure levels (28). Some specific beverages (e.g., red wine) may behave differently, but the evidence on this issue is scarce, and the score we used does not rank participants specifically on their red wine consumption (29).

Another explanation related to the Mediterranean diet score is that overall consumption of dairy products was indirectly assumed to be detrimental for blood pressure. However, consumption of low-fat dairy foods was part of the successful DASH combination diet (27), and other studies have suggested beneficial effects of consumption of low-fat dairy products (but not whole-fat dairy products) (30–33). Perhaps a more sensible approach to defining a score for hypertension prevention would be to use a score similar to the one proposed by Trichopoulou et al. (3) but exclude low-fat dairy products from the dairy products group. In any case, we acknowledge that the specific intake of low-fat dairy products (not intake of total dairy products) was in fact slightly higher among those of our participants who scored highest on the Mediterranean food pattern. Another modification could consist of weighting red wine consumption positively but not consumption of other alcoholic beverages, since red wine could be more likely to confer cardiovascular benefits than white wine or other alcoholic beverages (29, 34–36). Nevertheless, we decided not to modify the well-known and widely used score proposed by Trichopoulou et al. (3), to improve consistency with previous assessments. Besides, this score preserves well the classical concept of the Mediterranean diet as it was originally defined by Keys and Grande (37)—as the traditional dietary pattern found in olive-growing areas of Crete, Greece, and southern Italy in the late 1950s and early 1960s.

Consumption of MUFA and PUFA in our cohort participants did not increase across categories of adherence to the Mediterranean diet. The Mediterranean diet index developed by Trichopoulou et al. (3) does not include total MUFA but includes the MUFA:SFA ratio. Therefore, a higher MUFA:SFA ratio could be explained by decreased SFA intake, not only by increased MUFA intake. The main determinant of an increased MUFA:SFA ratio across levels of Mediterranean diet adherence in our cohort was decreased SFA intake. MUFA and PUFA consumption are believed to have cardioprotective effects, and the fact that their consumption did not increase across levels of adherence to the Mediterranean diet might partly explain our null findings. However, additional analyses showed no important relation between MUFA or PUFA intake and hypertension, although a certain (not statistically significant) trend suggesting an inverse association between MUFA and incident hypertension was observed.

In summary, our results do not support an association between the classical Mediterranean dietary pattern and the risk of hypertension. The observation of lower age-related changes in systolic and diastolic blood pressure among participants with higher adherence to the Mediterranean diet deserves further attention.

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REFERENCES

1. Lawes CM, Vander Hoorn S, Rodgers A, et al. Global burden of blood-pressure-related disease, 2001. *Lancet*. 2008; 371(9623):1513–1518.
2. Stamler J, Stamler R, Neaton JD. Blood pressure, systolic and diastolic, and cardiovascular risks. US population data. *Arch Intern Med*. 1993;153(5):598–615.
3. Trichopoulou A, Costacou T, Bamia C, et al. Adherence to a Mediterranean diet and survival in a Greek population. *N Engl J Med*. 2003;348(26):2599–2608.
4. Trichopoulou A, Bamia C, Norat T, et al. Modified Mediterranean diet and survival after myocardial infarction: The EPIC-Elderly Study. *Eur J Epidemiol*. 2007;22(12):871–881.
5. Willett WC, Sacks F, Trichopoulou A, et al. Mediterranean diet pyramid: a cultural model for healthy eating. *Am J Clin Nutr*. 1995;61(6 suppl):1402S–1406S.
6. Martínez-González MA, Fernández-Jarne E, Serrano-Martínez M, et al. Mediterranean diet and reduction in the risk of a first acute myocardial infarction: an operational healthy dietary score. *Eur J Nutr*. 2002;41(4):153–160.
7. Estruch R, Martínez-González MA, Corella D, et al. Effects of a Mediterranean-style diet on cardiovascular risk factors: a randomized trial. *Ann Intern Med*. 2006;145(1):1–11.
8. Nuñez-Cordoba JM, Alonso A, Beunza JJ, et al. Role of vegetables and fruits in Mediterranean diets to prevent hypertension. *Eur J Clin Nutr*. 2008;Feb 27 [Epub ahead of print].
9. Tortosa A, Bes-Rastrollo M, Sanchez-Villegas A, et al. Mediterranean diet inversely associated with the incidence of metabolic syndrome: the SUN prospective cohort. *Diabetes Care*. 2007;30(11):2957–2959.
10. Martínez-González MA, de la Fuente-Arrillaga C, Nunez-Cordoba JM, et al. Adherence to Mediterranean diet and risk of developing diabetes: prospective cohort study. *BMJ*. 2008; 336(7657):1348–1351.
11. Seguí-Gómez M, de la Fuente C, Vázquez Z, et al. Cohort profile: the 'Seguimiento Universidad de Navarra' (SUN) study. *Int J Epidemiol*. 2006;35(6):1417–1422.
12. Martin-Moreno JM, Boyle P, Gorgojo L, et al. Development and validation of a food frequency questionnaire in Spain. *Int J Epidemiol*. 1993;22(3):512–519.
13. Mataix Verdú J. *Tabla de Composición de Alimentos Españoles*. 4th ed. Granada, Spain: Universidad de Granada; 2003.
14. Moreiras O, Carbajal A, Cabrera L, et al. *Tablas de Composición de Alimentos*. 9th ed. Madrid, Spain: Editorial Pirámide; 2005.

15. Ainsworth BE, Haskell WL, Whitt MC, et al. Compendium of physical activities: an update of activity codes and MET intensities. *Med Sci Sports Exerc*. 2000;32(9 suppl): S498–S504.
16. Bes-Rastrollo M, Pérez Valdivieso JR, Sánchez-Villegas A, et al. Validación del peso e indice de masa corporal auto-declarados de los participantes de una cohorte de graduados universitarios. *Rev Esp Obes*. 2005;3(6):183–189.
17. Martínez-González MA, López-Fontana C, Varo JJ, et al. Validation of the Spanish version of the physical activity questionnaire used in the Nurses' Health Study and the Health Professionals' Follow-up Study. *Public Health Nutr*. 2005; 8(7):920–927.
18. Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA*. 2003;289(19):2560–2572.
19. Alonso A, Beunza JJ, Delgado-Rodríguez M, et al. Validation of self reported diagnosis of hypertension in a cohort of university graduates in Spain [electronic article]. *BMC Public Health*. 2005;5:94.
20. Willett WC. Issues in analysis and presentation of dietary data. In: Willett WC, ed. *Nutritional Epidemiology*. 2nd ed. New York, NY: Oxford University Press; 1998:321–346.
21. Kristal AR, Peters U, Potter JD. Is it time to abandon the food frequency questionnaire? *Cancer Epidemiol Biomarkers Prev*. 2005;14(12):2826–2828.
22. Lawes CM, Vander Hoorn S, Law MR, et al. Blood pressure and the global burden of disease 2000. Part II: estimates of attributable burden. *J Hypertens*. 2006;24(3):423–430.
23. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med*. 2001;344(1): 3–10.
24. Appel LJ, Champagne CM, Harsha DW, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. *JAMA*. 2003;289(16):2083–2093.
25. Elmer PJ, Obarzanek E, Vollmer WM, et al. Effects of comprehensive lifestyle modification on diet, weight, physical fitness, and blood pressure control: 18-month results of a randomized trial. *Ann Intern Med*. 2006;144(7):485–495.
26. Rasmussen BM, Vessby B, Uusitupa M, et al. Effects of dietary saturated, monounsaturated, and n-3 fatty acids on blood pressure in healthy subjects. *Am J Clin Nutr*. 2006;83(2): 221–226.
27. Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. *N Engl J Med*. 1997;336(16): 1117–1124.
28. Dickinson HO, Mason JM, Nicolson DJ, et al. Lifestyle interventions to reduce raised blood pressure: a systematic review of randomized controlled trials. *J Hypertens*. 2006;24(2): 215–233.
29. Martínez-González MA, Sánchez-Villegas A. The emerging role of Mediterranean diets in cardiovascular epidemiology: monounsaturated fats, olive oil, red wine or the whole pattern? *Eur J Epidemiol*. 2004;19(1):9–13.
30. Alonso A, Beunza JJ, Delgado-Rodríguez M, et al. Low-fat dairy consumption and reduced risk of hypertension: the Seguimiento Universidad de Navarra (SUN) cohort. *Am J Clin Nutr*. 2005;82(5):972–979.
31. Wang L, Manson JE, Buring JE, et al. Dietary intake of dairy products, calcium, and vitamin D and the risk of hypertension in middle-aged and older women. *Hypertension*. 2008;51(4): 1073–1079.
32. Djoussé L, Pankow JS, Hunt SC, et al. Influence of saturated fat and linolenic acid on the association between intake of dairy products and blood pressure. *Hypertension*. 2006;48(2): 335–341.
33. Toledo E, Delgado-Rodríguez M, Estruch R, et al. Low-fat dairy products and blood pressure: follow-up of 2290 older persons at high cardiovascular risk participating in the PREDIMED study. *Br J Nutr*. 2008;20:1–9.
34. Renaud S, de Lorgeril M. Wine, alcohol, platelets, and the French paradox for coronary heart disease. *Lancet*. 1992; 339(8808):1523–1526.
35. Criqui MH, Ringel BL. Does diet or alcohol explain the French paradox? *Lancet*. 1994;344(8939–8940):1719–1723.
36. Opie LH, Lecour S. The red wine hypothesis: from concepts to protective signalling molecules. *Eur Heart J*. 2007;28(14): 1683–1693.
37. Keys A, Grande F. Role of dietary fat in human nutrition. III. Diet and the epidemiology of coronary heart disease. *Am J Public Health Nations Health*. 1957;47(12):1520–1530.