European Journal of Clinical Nutrition (2009) 63, 605–612

www.nature.com/ejcn

ORIGINAL ARTICLE

Role of vegetables and fruits in Mediterranean diets to prevent hypertension

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Background/Objectives: Several studies support the effectiveness of increasing the consumption of fruits and vegetables (F&V) to prevent hypertension. However, none of them have been conducted in a Mediterranean setting. The aim of this study was to assess the association between F&V consumption and the risk of hypertension.
Subjects/Methods: A prospective Mediterranean study (the SUN cohort), including 8594 participants aged 20–95 years (mean, 41.1) with median follow-up of 49 months.
Results: Analyses according to the joint classification by olive oil and F&V consumption showed a significant inverse relation between F&V consumption and the risk of hypertension only among participants with a low olive oil consumption (<15 g per day). Also, tests for trend were significant only in the low olive oil intake stratum.
Conclusions: We found a statistically significant interaction ($P = 0.01$) between olive oil intake and F&V consumption. These data suggest a sub-additive effect of both food items.
European Journal of Clinical Nutrition (2009) **63,** 605–612; doi:10.1038/ejcn.2008.22; published online 27 February 2008

Keywords: fruit; vegetable; hypertension; olive oil; Mediterranean diet; prospective studies

Introduction

High blood pressure (HBP) has a high prevalence in many populations and it is associated to an excess risk of myocardial infarction, heart failure, stroke and kidney disease (Chobanian *et al*., 2003). As a result, HBP accounts for the greatest proportion of attributable deaths and represents the second most important global risk factor for the loss of disability-adjusted life years (Lopez *et al*., 2006).

The role of diet seems essential in the prevention of hypertension (Appel *et al*., 2006). Dietary trials (Appel *et al*., 1997; John *et al*., 2002) and observational studies (Psaltopoulou *et al*., 2004) have provided evidence to support the effectiveness of increasing the consumption of plant foods (especially vegetables and fruits) to decrease the risk of developing hypertension. Olive oil (Ferrara *et al*., 2000; Perona *et al*., 2004; Covas *et al*., 2006; Estruch *et al*., 2006) has been also suggested as an effective means to reduce blood pressure (BP) levels among hypertensives and to prevent the incidence of hypertension among normotensives (Alonso and Martinez-Gonzalez, 2004a; Perez-Jimenez *et al*., 2005).

Consequently, the traditional Mediterranean diet (rich in both olive oil and plant foods) potential to prevent the development of hypertension has been considered. However, in a population where olive oil is consumed in high amounts, the protection afforded by fruits and vegetables (F&V) may be less apparent than in other settings. These subadditive effects have been also reported for sodium and potassium in trials where the sum of the effects of each intervention separately was higher than the joint effect of

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Contributors: JMN-C and MAM-G had full access to all the data in the study and took responsibility for the integrity of the data and the accuracy of analyses. All authors participated in the conception and design of the study, and collection and assembly of data. JMN-C and MAM-G performed the statistical analysis. JMN-C, AA and MAM-G drafted the manuscript. Critical revision of the manuscript for important intellectual content was made by all authors. All authors read and approved the final paper.
Received 22 September 2007; revised 16 January 2008; accepted 30 January 2008; published online 27 February 2008

the two interventions together (Appel *et al.*, 1997, 2003, 2006). A suggestion for a lower effect of plant-food consumption on BP when monounsaturated fatty acid (MUFA) intake was high was previously reported by our group in a cross-sectional assessment of a Mediterranean population (Alonso *et al.*, 2004b). On the other hand, the European Prospective Investigation into Cancer and Nutrition-Greece group (Psaltopoulou *et al.*, 2004) reported that an inverse association between vegetable consumption and systolic blood pressure (SBP) was lost when the estimate was adjusted for olive oil consumption.

We assessed the relationship between the consumption of F&V and the incidence of hypertension in a prospective Mediterranean study after a median follow-up of 49 months.

Materials and methods

The Seguimiento University of Navarra cohort

The Seguimiento University of Navarra (SUN) Project is a dynamic cohort whose recruitment began in December 1999, with the main objective of studying the role of diet in the prevention of cardiovascular disease (CVD), obesity, diabetes and hypertension. A detailed description of the methods has been reported in detail elsewhere (Segui-Gomez *et al.*, 2006). Briefly, a mailed questionnaire was sent to all alumni of the University of Navarra and other university graduates in Spain. After the baseline assessment, participants receive biennial mailed follow-up questionnaires collecting a wide variety of information about diet, lifestyle, risk factors and medical conditions. Up to five mails were sent to nonrespondents. In June 2006, the SUN cohort included 13 631 participants who had been recruited at least 2 years ago. Among them, 12 168 had received all five mails requesting their follow-up questionnaires, and 10 940 of them completed their follow-up assessments (retention rate, 90%).

Dietary habits were assessed at baseline using a semi-quantitative food-frequency questionnaire with 136 items, previously validated in Spain (Martin-Moreno *et al.*, 1993) The questionnaire included 13 and 11 items for F&V consumption, respectively. We used the specified serving size for each item in the questionnaire to calculate the total servings per day of F&V for each participant. These serving sizes were specified in the food-frequency questionnaire taking into account the typical patterns of consumption in Spain.

The validity of self-reported weight and self-reported leisure-time physical activity in the SUN cohort has been previously reported (Bes-Rastrollo *et al.*, 2005; Martinez-Gonzalez *et al.*, 2005; Bes-Rastrollo *et al.*, 2006).

The study protocol has been approved by the Institutional Review Board of the University of Navarra. The response to the initial questionnaire was considered as an informed consent to participate in the study.

Hypertension

Incidence of hypertension was defined by self-reported responses. The validity of these self-reports has been shown to be sufficiently high when we compared it with objective measurements of BP in a random subsample of the cohort (Alonso *et al.*, 2005).

We requested to those participants who had completed a 6-year follow-up period to report their BP level as an open question included in the 6-year follow-up questionnaires. We used these values for analyses considering SBP and diastolic blood pressure (DBP) as continuous variables.

For the analyses, we excluded 745 participants who reported CVD at baseline and 1912 who reported at baseline either high BP levels ($\geqslant$140 mm Hg systolic and/or $\geqslant$90 mm Hg diastolic), a medical diagnosis of hypertension or to be under antihypertensive medication. In addition, we excluded 664 participants who had extreme caloric intakes (total energy intake greater than 4200 kcal per day (17 585 kJ per day) or less than 800 kcal per day (3349 kJ per day) for men, or greater than 3800 kcal per day (15 910 kJ per day) or less than 500 kcal per day (2093 kJ per day) for women).

Moreover, we excluded 194 participants with missing data for some of the covariates. After excluding those participants who met at least one of the previous exclusion criteria ($n = 2346$), 8594 participants remained available for analysis.

Statistical analysis

Analyses of hypertension risk were based on cumulative incidence rates. We conducted a multivariable Cox's regression analysis including 8594 SUN cohort participants to evaluate the association between consumption of servings per day of vegetables and fruit and incident hypertension. Hazard ratios (HRs) of hypertension and their 95% confidence intervals (95% CI) were estimated by comparing each category of intake with respect to the lowest category (<1 serving per day). We examined separately the association between incidence of hypertension and servings per day of vegetables, servings per day of fruits and servings per day of both F&V.

To test for linear trends, the median intake of a particular food in each category was assigned to all subjects in that same category, treating this new variable as continuous in the multivariable Cox regression analyses.

We repeated also all the analyses after stratifying by gender, age (<50, $\geqslant$50 years), body mass index (BMI) (<25, $\geqslant$25 kg m^{-2}) and olive oil consumption (cutoff point, energy-adjusted median; <15 g per day; $\geqslant$15 g per day) in order to assess effects within subgroups. We introduced product-terms to assess effect modification (interaction) by olive oil intake, gender, age and BMI.

We additionally repeated all the analyses using the consumption of F&V measured in grams per day, after adjusting it for total energy intake using the residual method.

In the subset of participants who completed the 6-year follow-up assessment, we computed adjusted means of SBP and DBP after 6-year follow-up according to categories of baseline consumption of F&V. We adjusted these means for age, gender and baseline BMI, using generalized linear models and analysis of covariance.

All reported *P*-values are derived from two-sided hypotheses and we considered significant *P*-values less than the conventional cutoff level of 0.05. All statistical analyses were performed using SPSS 14 software (SPSS Inc., Chicago, IL, USA).

Results

During the follow-up period (median, 49.3 months), we observed 426 cases of hypertension among 8594 participants (3256 men and 5338 women) initially free of hypertension. Table 1 shows the distribution of the characteristics of participants according to F&V consumption.

Cumulative incidence of hypertension showed an increase from 3.4% for persons aged 50 years or younger to 16.1% for those aged 60 years. Baseline BMI was significantly associated with an increased risk of hypertension (multivariate-adjusted HR, 2.66; 95% CI, 1.84–3.84) for baseline BMI $>30\,kg\,m^{-2}$ and for those with BMI between 25 and $30\,kg\,m^{-2}$ (HR, 1.76; 95% CI, 1.41–2.20), as compared with those with BMI <25. A positive association between alcohol consumption and the risk of hypertension was also found at intakes $\geqslant 30$ g per day of alcohol. Family history of hypertension (hypertension in a first-degree relative at baseline) was associated with an elevated risk of incident hypertension (HR, 1.55; 95% CI, 1.28–1.89) during the follow-up period.

We assessed the association of vegetables, categorized in five levels of servings per day, with the risk of incident hypertension (Table 2). Although the point estimate for the HR was lower in the category with the highest consumption, no statistically significant association between servings per day of vegetables consumption and hypertension was apparent. Tests for trend were not statistically significant.

We did not find any significant association between servings per day of fruits and the risk of hypertension (Table 3), though, as with vegetable consumption, the lower point estimate corresponded to the highest consumption category.

We further investigated the association of vegetables and fruits consumption with the risk of hypertension by combining the consumption of both vegetables and fruits together and building four categories of servings per day of

Table 1 Distribution of potential confounding variables across servings per day of F&V consumption[a]

F&V, servings per day	*⩽2*	*2.1–4*	*4.1–4.99*	*⩾5*
Participants (*n*)	1080	3169	1443	2902
Age (y)	38.9 (10.1)	40.4 (10.4)	41.9 (11.0)	42.1 (11.8)
Sex (% female)	48.4	56.2	65.6	72.1
BMI ($kg\,m^{-2}$)	23.3 (3.5)	23.1 (3.3)	22.9 (3.2)	22.8 (3.1)
Physical activity (MET h per week)	18.9 (18.1)	20.9 (19.3)	22.4 (18.4)	25.8 (24.1)
Hypercholesterolemia (%)	10.2	12.8	12.5	13.5
Diabetes (%)	0.5	0.7	0.7	1.7
Family history of hypertension (%)	30.8	34.0	35.3	37.0
Smoking status (%)				
Never	44.6	47.2	48.2	49.8
Former	34.0	28.3	24.5	22.4
Current	21.4	24.4	27.3	27.8
Alcohol intake (g per day)	6.9 (11.3)	6.5 (9.5)	6.1 (8.7)	5.4 (8.0)
Sodium intake (g per day)	3.3 (2.4)	3.5 (2.3)	3.5 (2.3)	3.5 (2.2)
Potassium intake (g per day)	3.0 (0.9)	4.3 (0.8)	4.8 (0.9)	6.1 (1.5)
Magnesium intake (mg per day)	292 (94)	367 (86)	422 (89)	508 (123)
Fiber intake (g per day)	13.8 (5.8)	21.3 (6.1)	27.5 (6.4)	38.1 (12.6)
Caffeine intake (g per day)	44.1 (43)	45.3 (39.3)	44.8 (39.7)	43.5 (39.2)
Olive oil (g per day)	14.0 (15.0)	17.8 (14.9)	19.3 (15.1)	22.1 (16.0)
Low-fat dairy (g per day)	140 (208)	172 (219)	211 (246)	245 (263)
Total energy intake (kJ per day)	8650 (2834)	9743 (2629)	10 279 (2554)	11 091 (2583)
Carbohydrates (% energy intake)	40.2 (8.5)	41.7 (7.0)	42.6 (6.4)	45.3 (7.2)
Protein (% energy intake)	17.8 (4.6)	17.9 (3.1)	18.1 (3.1)	18.0 (3.0)
Lipids (% energy intake)	39.7 (7.3)	38.4 (6.2)	37.5 (5.9)	35.3 (6.4)
SFA (% energy intake)	14.5 (3.8)	13.5 (3.0)	12.8 (2.8)	11.6 (3.0)
MUFA (% energy intake)	16.8 (4.5)	16.4 (3.6)	16.1 (3.5)	15.3 (3.6)
PUFA (% energy intake)	5.7 (1.9)	5.5 (1.6)	5.4 (1.6)	5.0 (1.5)

Abbreviations: BMI, body mass index; F&V, fruit and vegetable; h, hour; kg, kilogram; kJ, kilojoule; MET, metabolic equivalents; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid; SFA, saturated fat.
[a]Values are expressed as means (standard deviation) unless otherwise stated.

Table 2 Hazard ratios (95% CI) of hypertension according to servings per day of vegetable consumption in the SUN cohort

Servings per day of vegetables	*⩽1*	*1.1–2*	*2.1–3*	*3.1–4*	*>4*	P *for trend*
N	1258	3208	2350	1067	711	
Incident cases	64	169	114	52	31	
Persons-years	4906	12 511	9165	4161	2773	
Rate per 1000	13.0	13.5	12.4	12.5	11.2	
HR (95% CI)[a]	1 (ref.)	1.01 (0.75–1.34)	0.93 (0.69–1.27)	0.96 (0.67–1.39)	0.85 (0.56–1.31)	0.36
Adjusted HR (95% CI)[b]	1 (ref.)	1.04 (0.78–1.38)	0.98 (0.72–1.33)	1.05 (0.72–1.51)	0.92 (0.60–1.43)	0.74
Multivariate HR (95% CI)[c]	1 (ref.)	1.00 (0.74–1.34)	0.92 (0.66–1.27)	1.03 (0.70–1.52)	0.87 (0.55–1.39)	0.61

Abbreviations: CI, confidence intervals; HR, hazard ratio; ref., reference; SUN, Seguimiento University of Navarra.
[a]Unadjusted model.
[b]Adjusted for age and gender.
[c]Adjusted for age, gender, total energy intake, BMI, physical activity, alcohol, family history of hypertension, sodium intake, low-fat dairy intake, whole grains intake, fish intake and smoking.

Table 3 Hazard ratios (95% CI) of hypertension according to servings per day of fruit consumption in the SUN cohort

Servings per day of fruits	*⩽1*	*1.1–2*	*2.1–3*	*3.1–4*	*>4*	P *for trend*
N	2033	2701	1754	932	1174	
New cases	103	127	92	54	54	
Persons-years	7929	10 534	6841	3635	4579	
Rate per 1000	13.0	12.1	13.4	14.9	11.8	
HR (95% CI)[a]	1 (ref.)	0.92 (0.71–1.19)	1.05 (0.79–1.39)	1.13 (0.81–1.57)	0.93 (0.67–1.29)	0.96
Adjusted HR (95% CI)[b]	1 (ref.)	0.89 (0.68–1.15)	0.96 (0.72–1.28)	1.06 (0.76–1.49)	0.87 (0.62–1.21)	0.66
Multivariate HR (95% CI)[c]	1 (ref.)	0.86 (0.66–1.13)	0.94 (0.70–1.27)	1.02 (0.72–1.45)	0.85 (0.59–1.22)	0.70

Abbreviations: CI, confidence intervals; HR, hazard ratio; ref., reference; SUN, Seguimiento University of Navarra.
[a]Unadjusted model.
[b]Adjusted for age and gender.
[c]Adjusted for age, gender, total energy intake, BMI, physical activity, alcohol, family history of hypertension, sodium intake, low-fat dairy intake, whole grains intake, fish intake and smoking.

F&V (Table 4). The HR of hypertension for the highest versus the lowest category of F&V was lower than 1, but the confidence interval included the null value. Results were substantially unchanged when we controlled for baseline diabetes and hyperlipidemia, when we excluded the patients with diabetes at baseline or when we also excluded participants with cancer at baseline. Similar results were found when we used quintiles of energy-adjusted consumption of F&V (gram per day, using the residuals method) instead of using units of servings per day (data not shown).

We also repeated the analyses after excluding participants who had not checked their BP during the follow-up period. The multivariate-adjusted HR for those in the highest category of vegetable consumption as compared with the lowest one was 0.95 (95% CI, 0.59–1.51). For fruits consumption, the HR obtained was 0.79 (95% CI, 0.55–1.15) when comparing extreme categories. Finally, the comparison of extreme categories of servings of joint F&V consumption yielded an HR, 0.77 (95% CI, 0.55–1.09).

We examined the association between F&V consumption and hypertension risk according to intake of energy-adjusted olive oil consumption (Table 5). We found a significant inverse relation between F&V consumption and the risk of hypertension only among participants with a low olive oil consumption (<15 g per day). The test for trend in this group was statistically significant. The interaction between olive oil and F&V was statistically significant (P for the interaction term = 0.01), suggesting a selective beneficial effect of F&V restricted only to participants with a lower olive oil consumption.

Subgroup analyses by BMI, age and sex provided similar results as compared to those from the whole sample.

Among participants who had completed the 6-year follow-up assessment ($n = 1461$), 1137 provided their SBP and 1132 provided their DBP. The correlations between self-reported BP at baseline and self-reported BP after 6-year follow-up were 0.53 (95% CI, 0.48–0.57; $P < 0.001$) for SBP and 0.43 (95% CI, 0.38–0.48; $P < 0.001$) for DBP. The correlation between SBP and DBP at baseline was 0.66 (95% CI, 0.65–0.67) and after 6-year follow-up it was also 0.66 (95% CI, 0.63–0.69).

Among normotensive individuals, baseline BP predicted the incidence of hypertension during the follow-up period: multivariate-adjusted HR, 3.2 (95% CI, 2.1–5.0) and 8.6 (95% CI, 5.3–13.9) for the second and third tertile of baseline SBP and 1.8 (95% CI, 1.3–2.4) and 4.3 (95% CI, 3.0–6.0) for the second and third tertiles of baseline DBP. Participants with high BP levels [SBP (131–139) or DBP (81–89)] at baseline had

Table 4 Hazard ratios (95% CI) of hypertension according to servings per day of fruits and vegetables (F&V) in the SUN Cohort

Servings per day of F&V	*⩽2*	*2.1–4*	*4.1–4.9*	*⩾5*	P *for trend*
N	1080	3169	1443	2902	
Cases	61	161	76	132	
Persons-years	4212	12 359	5628	11 318	
Rate per 1000	14.5	13.0	13.5	11.7	
HR (95% CI)[a]	1 (ref.)	0.90 (0.67–1.21)	0.94 (0.67–1.32)	0.82 (0.61–1.12)	0.19
Adjusted HR (95% CI)[b]	1 (ref.)	0.90 (0.67–1.20)	0.93 (0.66–1.31)	0.83 (0.61–1.13)	0.24
Multivariate HR (95% CI)[c]	1 (ref.)	0.86 (0.63–1.16)	0.86 (0.60–1.24)	0.78 (0.55–1.10)	0.22

Abbreviations: CI, confidence intervals; F&V, fruit and vegetable; HR, hazard ratio; ref., reference; SUN, Seguimiento University of Navarra.
[a]Unadjusted model.
[b]Adjusted for age and gender.
[c]Adjusted for age, gender, total energy intake, BMI, physical activity, alcohol, family history of hypertension, sodium intake, low-fat dairy intake, whole grains intake, fish intake and smoking.

Table 5 Hazard ratios (95% CI) of hypertension according to the joint classification by energy-adjusted olive oil consumption (cutoff point = median consumption) and by the consumption of F&V in the SUN Cohort[a]

Servings per day of F&V	*⩽2*	*2.1–4.0*	*4.1–4.9*	*⩾5*	P *for trend*
Low olive oil (<15 gram per day)					
N	629	1623	737	1295	
Cases	40	89	46	50	
Persons-years	2453	6330	2874	5051	
Rate per 1000	16.3	14.1	16.0	9.9	
Multivariate HR (95% CI)[b]	1 (ref.)	0.88 (0.60–1.30)	0.90 (0.57–1.41)	0.56 (0.35–0.89)	0.008
High olive oil (⩾15 gram per day)					
N	451	1546	706	1607	
Cases	20	70	29	82	
Person*Y	1759	6029	2753	6267	
Rate per 1000	11.4	11.6	10.5	13.1	
Multivariate HR (95% CI)[b]	1 (ref.)	0.88 (0.52–1.49)	0.84 (0.46–1.55)	1.12 (0.64–1.96)	0.249

Abbreviations: CI, confidence intervals; F&V, fruit and vegetable; HR, hazard ratio; SUN, Seguimiento University of Navarra.
[a]Interaction (product-term: olive oil × F&V) $P = 0.01$.
[b]Adjusted for age, gender, total energy intake, BMI, physical activity, alcohol, family history of hypertension, sodium intake, low-fat dairy intake, whole grains intake, fish intake and smoking.

Table 6 Association between fruit or vegetable consumption and average blood pressure levels in the 6-year follow-up questionnaire. General linear models. Adjusted means[a] (95% confidence intervals) ($n = 1195$)

Servings per day	*Fruits*		*Servings per day*	*Vegetables*	
	Systolic BP	*Diastolic BP*		*Systolic BP*	*Diastolic BP*
⩽1	115.1 (113.6–116.5)	70.8 (69.7–71.9)	⩽1	113.5 (111.8–115.3)	70.2 (68.8–71.5)
1.1–2	114.8 (113.6–116.1)	70.2 (69.2–71.1)	1.1–2	115.0 (113.9–116.1)	70.9 (70.0–71.7)
2.1–3	115.1 (113.6–116.6)	71.4 (70.2–72.5)	2.1–3	114.9 (113.4–116.3)	69.9 (68.9–71.0)
3.1–4	114.5 (112.4–116.6)	70.5 (68.9–72.1)	3.1–4	115.8 (113.7–117.9)	69.7 (68.1–71.3)
⩾4	113.5 (111.5–115.4)	68.1 (66.7–69.6)	⩾4	113.5 (110.9–116.1)	69.8 (67.8–71.8)
P (ANCOVA)	0.71	0.01		0.40	0.53

Abbreviations: ANCOVA, analysis of covariance; BMI, body mass index; BP, blood pressure.
[a]Adjusted for age, gender and BMI.

a higher risk of developing hypertension when compared to those with lower levels of BP (HR, 3.24; 95% CI, 2.61–4.01; $P < 0.001$).

We estimated the association between baseline BMI and BP at 6-year follow-up using a linear regression models. An increase of one standard deviation in baseline BMI was associated with higher levels of SBP and DBP in the future (regression coefficients, 1.9 mm Hg; 95% CI, 1.1–2.1; $P < 0.001$ for SBP and 1.7; 95% CI, 0.7–1.9; $P < 0.001$ for DBP).

We analyzed the association between baseline fruits or vegetables consumption and average BP levels after 6 years of follow-up (Table 6). With only one exception (diastolic BP

Table 7 Association between F&V consumption and average blood pressure levels in the 6-year follow-up questionnaire according to olive oil consumption. General linear models. Adjusted means[a] (95% confidence intervals) ($n=1195$)

Servings per day of F&V	*Low olive oil consumption (<median)*		*High olive oil consumption (>median)*	
	Systolic BP	*Diastolic BP*	*Systolic BP*	*Diastolic BP*
⩽2	115.4 (112.9–117.9)	70.7 (68.9–72.4)	114.0 (110.3–117.7)	70.1 (67.1–73.1)
2.1–4	115.3 (113.7–116.9)	70.7 (69.5–71.8)	114.4 (112.8–115.9)	71.0 (69.7–72.2)
4.1–4.9	114.9 (112.5–117.3)	70.1 (68.3–71.8)	113.0 (110.5–115.4)	71.6 (69.6–73.5)
⩾5	113.9 (112.1–115.8)	69.4 (68.1–70.8)	115.5 (113.7–117.2)	69.8 (68.3–71.2)
Difference (lower–upper)	−1.5	−1.3	+1.5	−0.3
P (ANCOVA)	0.69	0.54	0.41	0.41

Abbreviations: ANCOVA, analysis of covariance; BMI, body mass index; BP, blood pressure.
[a]Adjusted for age, gender and BMI.

according to vegetables consumption), the lowest mean BP was found always among participants with the highest consumption of fruits and vegetables, although only the inverse association between fruit and DBP was statistically significant.

The association of F&V consumption stratified by levels of baseline olive oil consumption (using the median as cutoff point) and levels of BP at 6 years was not statistically significant (Table 7). Differences between the highest category of servings per day of F&V and the lowest category were more obvious among participants with low baseline olive oil consumption than among those with high olive oil consumption. The *P*-value for interaction (olive oil by F&V) was not statistically significant ($P=0.96$ for DBP and $P=0.50$ for SBP).

Finally, restricting the analysis to those participants followed-up for ⩾6 years and excluding those with medically diagnosed incident hypertension, the multivariate-adjusted relative risk of having after 6-year follow-up high BP levels (outcome, SBP⩾140 or DBP⩾90 mm Hg but not a diagnosis of hypertension) was 0.59 (95% CI, 0.25–1.39) for those with ⩾5 servings per day of F&V. No statistically significant interaction ($P=0.51$ for the interaction term) between olive oil and F&V servings was observed when we used high BP levels (⩾140/90) after 6-year follow-up as the outcome.

Discussion

We observed an inverse relation between servings per day of F&V consumption (⩾5 servings per day) and the incidence of hypertension only among those participants with a lower consumption of olive oil. This finding might seem to be inconsistent with previous results of other prospective epidemiological studies (Rouse *et al*., 1983; Margetts *et al*., 1986; Appel *et al*., 1997, 2003; Conlin *et al*., 2000; Moore *et al*., 2001; John *et al*., 2002; Ard *et al*., 2004; Miura *et al*., 2004; Elmer *et al*., 2006) Moreover, an inverse association between F&V consumption and prevalence of hypertension has been observed in the CARDIO2000 study, a Mediterranean case-control study (Panagiotakos *et al*., 2003a).

The ATTICA study has suggested that the consumption of a Mediterranean-type diet reduces rates of hypertension in the population, and may contribute to the control of hypertension at the population level (Panagiotakos *et al*., 2003b). Our study population, the SUN cohort, is relatively young as compared to other studies. It is plausible that the protection afforded by F&V on the risk of hypertension may be less apparent in a younger population, in which olive oil is consumed in higher amounts than that in other settings: individuals at lower risk of disease due to their exposure to healthy factors (such as olive oil intake) do not experience much additional benefit from exposure to other protective factors. On the other hand, the role of F&V consumption in the prevention of hypertension has not previously assessed with a prospective design study in a Mediterranean setting.

A limitation in our study is measurement error. Food-frequency questionnaires provide information from dietary habits that ordinarily show a good correlation with usual diet but this fact does not prevent a possible misclassification bias (Kristal *et al*., 2005). Nevertheless, our questionnaire has been previously validated and used in our cohort demonstrating a fair validity and reliability (Martin-Moreno *et al*., 1993). Moreover, measurement error could not explain the statistically significant inverse association between F&V and hypertension found within the stratum of low olive oil consumption, or the statistically significant test for interaction, since non-differential measurement error usually biases results toward the null value.

Reverse causation bias is very unlikely because the SUN cohort is a prospective cohort study. We excluded from our analyses individuals with diagnosed hypertension and those with prevalent CVD at baseline, whose diets are probably different due to their lifestyle modifications derived from diagnosis and medical advice. Also, when we excluded subjects with prevalent cancer or we controlled for baseline diabetes or hyperlipidemia the results did not materially change. An important limitation in our study is the self-reported diagnosis of HT. However, previous studies suggest the validity of our outcome measure (Ascherio *et al*., 1996; Tormo *et al*., 2000; Alonso *et al*., 2005). The correlation between BP levels at baseline and after a 6-year follow-up period also provides support for the validity of our methods.

Removing from the analyses those participants who had not checked their BP may avoid an underestimation of the effect of F&V on incident hypertension. Therefore, we also repeated the analyses restricting them to persons who had checked their BP during the follow-up period. Results of these analyses were not materially different from those including the entire cohort. Our results have shown a small nonsignificant beneficial inverse association between F&V and the risk of hypertension, even independently of olive oil consumption. It would be implausible to expect a strong reduction when the initial levels of BP are not high and the baseline risk is low.

Our study is the first prospective study conducted in a population following a Mediterranean-type food pattern that assessed the association between diet and incidence of hypertension. In this setting, further increments in the consumption of F&V may not lead to such a reduction in the risk of hypertension as it would be expected in other settings where olive oil is not the major fat for cooking and dressing salads or where lower absolute levels of consumption for legumes, nuts, fruits and vegetables are found.

Acknowledgements

We thank all members of the SUN Study Group for administrative, technical and material support. We thank participants of the SUN Study for continued cooperation and participation. The SUN Study has received funding from the Spanish Ministry of Health (Grants PI030678, PI040233, PI070240, RD06/0045, and G03/140), the Navarra Regional Government (PI141/2005) and the University of Navarra. The SUN Study has received funding from the Spanish Ministry of Health (Grants PI030678, PI040233, P1070240, RD06/0045, and G03/140), the Navarra Regional Government (PI141/2005) and the University of Navarra.

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