Olive Oil Consumption and Reduced Incidence of Hypertension: The SUN Study

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ABSTRACT: Olive oil, a major component of the Mediterranean diet, has been associated in some small clinical trials and cross-sectional studies with a reduction in blood pressure. The objective of this study was to assess the association of olive oil consumption with the incidence of hypertension in an epidemiologic cohort, the Seguimiento Universidad de Navarra (SUN) study. The SUN Project is a prospective cohort study whose members are all university graduates. The recruitment and follow-up of participants is made using mailed questionnaires. Diet was assessed using a semiquantitative food frequency questionnaire previously validated in Spain, with 136 items. Outcomes of interest were newly diagnosed cases of hypertension, as reported by participants in the follow-up questionnaires. Logistic regression models were fit to assess the risk of hypertension associated with olive oil consumption. For the present analysis, we have taken in consideration the first 6,863 participants, with at least 2 yr of follow-up. After a median follow-up time of 28.5 mon, the cumulative incidence of hypertension was 4.7% in men and 1.7% in women. A lower risk of hypertension was observed among participants with a higher olive oil consumption at baseline, but the results were not statistically significant ($P = 0.13$ for the linear trend test in the multivariate model). However, among men, the adjusted odds ratios (OR) (95% confidence intervals) of hypertension for the second to fifth quintiles of olive oil consumption, compared with the first quintile, were 0.55 (0.28–1.10), 0.75 (0.39–1.43), 0.32 (0.15–0.70), and 0.46 (0.23–0.94), respectively ($P = 0.02$ for linear trend). No association was found between olive oil consumption and the risk of hypertension among women. In conclusion, in a Mediterranean population, we found olive oil consumption to be associated with a reduced risk of hypertension only among men. The lack of association observed among women might be attributed to the overall lower incidence of hypertension found among females and the resulting lower statistical power.

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The adherence to traditional Mediterranean dietary patterns (MDP) has been associated in some studies with a reduced risk of coronary heart disease (1,2). One plausible biological mechanism that may explain this benefit is the protective effect of some components of traditional MDP against hypertension, a major risk factor for cardiac disease. For example, high fruit and vegetable consumption has been linked with a lower risk of hypertension and reduced blood pressure (3,4).

Another characteristic of the typical MDP is the elevated consumption of olive oil as the main source of added lipids. There are, however, scarce data relating olive oil to blood pressure or to the risk of hypertension. Some small studies conducted in healthy volunteers and hypertensive patients suggest a beneficial effect of olive oil on blood pressure (5–7). Additionally, a small clinical trial has shown a reduced need for blood pressure lowering drugs in hypertensive subjects receiving extra-virgin olive oil (8). Nevertheless, no large epidemiological studies conducted in Mediterranean countries have assessed the association between olive oil consumption and the risk of hypertension.

Using data from the Seguimiento Universidad de Navarra (University of Navarra Follow-up, SUN) study, a prospective cohort study in Spain, we tried to assess whether olive oil consumption, independent of consumption of other foods, was associated with a lower risk of hypertension.

METHODS

The SUN Project. The SUN Project is a prospective cohort study conducted in Spain. A detailed description of its methods has been published elsewhere (9). The recruitment of participants began in 2000, and remains open (the study design corresponds to a dynamic cohort). All members of the cohort are university graduates, mainly former students of the University of Navarra. Other participants have been recruited from the Nurses Professional Association of Navarra and from an insurance company (ACUNSA, Inc.). Recruitment and follow-up of participants are done through biennial mailed questionnaires. The study protocol has been approved by the Institutional Review Board of the University of Navarra. For the present analysis, we have taken into consideration the first 6,863 participants, with at least two years of follow-up.

Dietary assessment. Diet was assessed in the baseline questionnaire using a semiquantitative food-frequency questionnaire, previously validated in Spain (10). The questionnaire has 136 food items, and open-labeled questions for dietary supplement intake and other food items not included in the questionnaire. The questionnaire offered nine frequency categories of intake for each food item (from 6+ per day to never or almost never). In addition to particular questions regarding consumption of olive oil consumption used in frying, as a spread, or to season

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Abbreviations: CI, confidence interval; MDP, Mediterranean dietary patterns; MET, metabolic equivalents; MUFA, monounsaturated fatty acids; OR, odds ratio; SUN, Seguimiento Universidad de Navarra (University of Navarra Follow-up).

salads, the type of fat used in frying was specifically assessed. The biennial follow-up questionnaires also gathered information about changes in the habitual consumption of main components of the MDP, including olive oil. A dietitian updated the nutrient data bank using the latest available information included in the food composition tables for Spain (11).

Assessment of other covariates. The baseline questionnaire collected information about sociodemographic variables (age, sex, marital and occupational status), anthropometric measures (height, weight), smoking, physical activity during leisure time, sedentary lifestyle, and some clinical variables (medication use, past history of coronary heart disease, cancer, and other diseases).

Outcome ascertainment. In the baseline questionnaire, participants reported whether they had a history of medically diagnosed hypertension and their usual systolic and diastolic blood pressure (nine categories). In the follow-up questionnaire, individuals were asked to report whether they had received a physician's diagnosis of hypertension in the time between both questionnaires. Validity of self-reported hypertension has been shown to be appropriate in other similar settings (12, 13). In a sample of 63 participants of the SUN Study living in the metropolitan area of Pamplona, 31 reporting hypertension and 32 without a history of hypertension, there was a fair correlation between self-reported and measured systolic and diastolic blood pressure (Spearman's rho = 0.62 and 0.65, respectively). The negative predictive value was 94%, and the positive predictive value was 65%.

Statistical analysis. The main exposure of interest was olive oil consumption, adjusted for total energy intake using the residuals method (14) and taking total energy intake into account separately for women and men. Energy-adjusted olive oil consumption was divided into five categories, using quintiles as cutoff points. The main outcome variable was a new physician-made diagnosis of hypertension. This was defined as a self-reported physician-made diagnosis of hypertension in the follow-up questionnaire, with no report of a diagnosis of hypertension in the baseline questionnaire.

The cumulative incidence of hypertension was computed for each quintile of olive oil consumption. To avoid the confounding effect of other variables simultaneously associated with the outcome and the main exposure, we used nonconditional logistic regression modeling. The main known risk factors for hypertension were included in the final model. These potential confounders were age, gender, body mass index, physical activity during leisure time (metabolic equivalents [METS-h/week]), total energy intake, alcohol consumption, sodium intake, and calcium intake. In addition, models for each sex were run separately.

Tests for a linear trend in the relationship between olive oil consumption and risk of hypertension were obtained by assigning the median value for each quintile of olive oil consumption and modeling this variable as continuous in the logistic model.

RESULTS

The rate of follow-up for the first 7,650 participants in the cohort is 90%. The median follow-up time was 28.5 months. From the 6,863 respondents with data at baseline and at the first follow-up questionnaire, 658 were excluded due to prevalent hypertension at baseline and 632 because of extremely low or high caloric intakes (<400 kcal/day for women, <600 kcal/day for men, >3500 kcal/day for women, >4200 kcal/day for men). Finally, 5,573 participants were available for analysis, 3,384 women and 2,189 men. During the follow-up time, 161 incident cases of hypertension were identified among them (cumulative incidence 2.9%). The incidence was much lower in women than in men (1.7 vs. 4.7%). The characteristics of participants according to their quintiles of olive oil consumption are presented in Table 1, separately for men and women. Age and alcohol consumption were positively correlated with olive oil consumption, whereas sodium intake was inversely associated with it.

Odds ratios (OR) for incident hypertension in the whole sample are shown in Table 2. When we considered men and women together, in the age- and sex-adjusted analysis, olive oil was not associated with the incidence of hypertension. However, in the multivariate analysis, taking into consideration some known risk factors for hypertension, the fourth quintile of olive oil consumption was associated with a significantly decreased risk of hypertension, compared with the quintile with the lowest consumption.

Interestingly, after stratifying by sex, a clear inverse relationship between olive oil consumption and the risk of hypertension was apparent among male participants (Table 3). Men with the highest olive oil consumption, i.e., those in the fifth quintile, had a significantly lower risk of hypertension compared with those in the first quintile, as shown by the OR of 0.46 (95% confidence interval 0.23–0.94). Also, there was a significant linear trend for the association between olive oil consumption and the risk of hypertension ($P = 0.02$), suggesting a dose-response relationship between olive oil consumption and incidence of hypertension among men. In women, olive oil consumption was not associated with a change in the risk of hypertension. Further adjustment for fruit and vegetable consumption did not materially change the point estimates for the OR, and the linear trend continued to be statistically significant ($P = 0.03$).

DISCUSSION

In this prospective study, conducted in a Mediterranean population, those men with a higher olive oil consumption at baseline had a lower risk of developing hypertension, independently of other risk factors for this disorder. This relationship was not apparent among women. The lack of association observed among women could be attributed to the lower incidence of hypertension among females and consequently to lower statistical power. In fact, only 59 cases of incident hypertension were observed among women, thus hindering the ability to ascertain with confidence any association of weak magnitude.

To our knowledge, this is the first large epidemiological study showing an inverse association between olive oil consumption and the risk of hypertension. Some previous studies conducted in Mediterranean countries have shown a protective

TABLE 1
Distribution of Selected Variables Across Quintiles of Energy-Adjusted Olive Oil Consumption[a]

	Quintiles of energy-adjusted olive oil consumption					
Women	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	*P* for trend
N	676	677	677	677	677	
Energy-adjusted olive oil consumption (g/d) (median)	5.3	11.2	16.8	25.1	36.2	
Age (yr) (mean)	34.5	36.2	37.3	36.8	38.5	<0.001
Total energy intake (kcal/d)	2594.3	2204.0	2090.4	2446.0	2313.1	0.18
BMI (mean)	21.5	21.8	21.8	21.9	22.0	<0.001
Physical activity during leisure time in METs-h/wk (mean)	14.6	15.9	15.9	17.1	15.1	0.27
Alcohol consumption (g/d) (mean)	3.6	3.4	4.1	3.8	4.0	0.04
Sodium consumption (g/d) (mean)	4.1	3.1	2.8	3.1	2.8	<0.001
Calcium consumption (g/d) (mean)	1.4	1.2	1.2	1.4	1.2	0.009
Fruit consumption (g/d) (mean)	391.9	397.0	383.5	387.8	355.8	0.04
Vegetable consumption (g/d) (mean)	512.6	585.8	594.8	623.0	602.3	<0.001
Dietary fiber consumption (g/d) (mean)	33.7	28.0	27.0	31.3	30.8	<0.001
	Quintiles of energy-adjusted olive oil consumption					
Men	Q1 (lowest)	Q2	Q3	Q4	Q5 (highest)	*P* for trend
N	437	438	438	438	438	
Energy-adjusted olive oil consumption (g/d) (median)	4.0	9.0	13.3	19.1	32.4	
Age (yr) (mean)	39.6	42.0	43.7	43.0	44.4	<0.001
Total energy intake (kcal/d)	2858.2	2516.0	2227.3	2407.9	2631.2	<0.001
BMI (mean)	24.6	25.0	25.3	25.3	25.3	<0.001
Physical activity during leisure time in MET-h/wk (mean)	23.8	23.8	22.5	22.5	24.4	0.83
Alcohol consumption (g/d) (mean)	8.7	9.7	9.1	10.1	10.8	0.03
Sodium consumption (g/d) (mean)	4.9	4.0	3.5	3.7	3.4	<0.001
Calcium consumption (g/d) (mean)	1.4	1.2	1.1	1.1	1.2	<0.001
Fruit consumption (g/d) (mean)	296.3	309.2	294.9	299.7	302.8	0.93
Vegetable consumption (g/d) (mean)	388.7	442.4	470.7	490.4	543.8	<0.001
Dietary fiber consumption (g/d) (mean)	29.0	25.9	23.2	25.8	29.7	0.45

[a]BMI, body mass index; MET, metabolic equivalent.

effect of olive oil in relation to the development of nonfatal myocardial infarction (15) or coronary death (1,16). A possible explanation for this favorable effect in studies of coronary heart disease is the beneficial effect of olive oil on blood pressure. In some small studies and clinical trials, olive oil has been shown to have a lowering effect on blood pressure. For example, in a crossover clinical trial conducted on 16 hypertensive women, olive oil but not a high-oleic sunflower oil, was associated with a significant reduction in systolic and diastolic blood pressure (7). In another study, a diet enriched with olive oil, followed during a period of 5 wk, was associated with a reduced mean blood pressure in 42 individuals (18 women and 24 men) (6). More interestingly, in a double-blind, randomized cross-over clinical trial conducted on 23 hypertensive patients, a diet rich in monounsaturated FA (MUFA) from extra-virgin olive oil was associated with lower systolic and diastolic blood pressure, and also with a reduced need for antihypertensive medication when compared with a diet rich in PUFA (8). The authors of the study suggested that the beneficial effect of olive oil on blood pressure was not only associated with its MUFA content,

TABLE 2
Odds Ratios (OR) and 95% Confidence Intervals (CI) of Self-Reported Incident Hypertension According to Quintiles of Olive Oil Consumption in the SUN Study

	Quintiles of energy-adjusted olive oil consumption					
	Q1	Q2	Q3	Q4	Q5	*P* for trend
Participants (*N*)	1113	1115	1115	1115	1115	
Median olive oil consumption (g/d)	4.8	10.2	15.0	23.5	34.6	
New cases of hypertension, *N* (%)	32 (2.9)	26 (2.3)	41 (3.7)	30 (2.7)	32 (2.9)	
Age- and sex-adjusted OR (95% CI)	1 (ref.)	0.69 (0.40–1.17)	1.01 (0.62–1.64)	0.77 (0.46–1.29)	0.75 (0.45–1.25)	0.39
Multivariate OR (95% CI)[a]	1 (ref.)	0.61 (0.35–1.07)	0.83 (0.49–1.41)	0.55 (0.31–0.98)	0.63 (0.36–1.07)	0.13

[a]Non-conditional logistic regression model adjusted for age (in years), sex, BMI (defined as weight in kilograms divided by the square of height in meters), energy intake, alcohol consumption (in g/d), sodium intake (in mg/d), calcium intake (in g/d), and physical activity during leisure time (in METs-h/wk). SUN, Seguimiento Universidad de Navarra; for other abbreviations see Table 1.

TABLE 3
OR and 95% CI of Self-Reported Incident Hypertension According to Quintiles of Olive Oil Consumption in the SUN Study

	Quintiles of energy-adjusted olive oil consumption					
Women	Q1	Q2	Q3	Q4	Q5	*P* for trend
Participants (*N*)	676	677	677	677	677	
Median olive oil consumption (g/d)	5.3	11.2	16.8	25.1	36.2	
New cases of hypertension, *N* (%)	9 (1.3)	8 (1.2)	12 (1.8)	15 (2.2)	15 (2.2)	
Age-adjusted OR (95% CI)	1 (ref.)	0.78 (0.30–2.06)	1.04 (0.43–2.51)	1.45 (0.62–3.35)	1.26 (0.54–2.93)	0.27
Multivariate OR (95% CI)[a]	1 (ref.)	0.74 (0.27–2.02)	0.97 (0.38–2.45)	1.14 (0.47–2.78)	0.97 (0.40–2.36)	0.74

	Quintiles of energy-adjusted olive oil consumption					
Men	Q1	Q2	Q3	Q4	Q5	*P* for trend
Participants (*N*)	437	438	438	438	438	
Median olive oil consumption (g/d)	4.0	9.0	13.3	19.1	32.4	
New cases of hypertension, *N* (%)	23 (5.3)	18 (4.1)	29 (6.6)	15 (3.4)	17 (3.9)	
Age-adjusted OR (95% CI)	1 (ref.)	0.65 (0.34–1.23)	1.00 (0.56–1.78)	0.52 (0.26–1.01)	0.55 (0.28–1.05)	0.05
Multivariate OR (95% CI)[a]	1 (ref.)	0.55 (0.28–1.10)	0.75 (0.39–1.43)	0.32 (0.15–0.70)	0.46 (0.23–0.94)	0.02

[a]Nonconditional logistic regression model adjusted for age (in years), BMI (defined as weight in kilograms divided by square of height in meters), energy intake, alcohol consumption (in g/d), sodium intake (in mg/d), calcium intake (in g/d), and physical activity during leisure time (in MET-h/wk). For abbreviations see Tables 1 and 2.

but also with the high content of antioxidant polyphenols. In this same study, patients supplemented with sunflower oil did not experience a beneficial effect.

The mechanisms behind the protective role of olive oil for hypertension are not clear. MUFA intake could be associated with an increased sensitivity to insulin, producing a reduction in blood pressure (17). However, some authors suggest that other components of olive oil, such as the polyphenols mentioned, could be associated with lower blood pressure and a reduced risk of hypertension. In fact, some studies have shown a reduction of blood pressure following supplementation with antioxidants (18), although there are some inconsistencies on this issue (19). Another explanation for the beneficial effect of olive oil on blood pressure is its greater resistance to denaturation during the process of frying, with a lower production of polar compounds. In a cross-sectional study conducted in southern Spain on 538 persons, the amount of polar compounds in cooking oil was associated with hypertension, and a lower concentration of polar compounds was found in olive oil used for frying when compared with sunflower oil from the same source. In that study, individuals using olive oil for frying had a higher concentration of MUFA in plasma phospholipids, and this variable was inversely associated with the prevalence of hypertension (20). Another possible explanation of olive oil's antihypertensive effect involves molecules closely related to the main FA contained in olive oil. A strong blood pressure-reducing effect has recently been observed for 2-hydroxy-oleic acid in an experimental model (21).

Our study has important strengths. Its prospective design avoids the reverse-causation bias. Also, the follow-up rate is high. Additionally, all participants are university graduates, allowing a better understanding of the food-frequency questionnaire and increasing the internal validity of our findings. Diet has been assessed with a comprehensive tool, previously validated and used in similar settings.

There are some limitations in this analysis. Statistically significant results, using the traditional cutoff point of $P < 0.05$, were found only after several analyses (whole sample, women, and men), increasing the possibility of a false positive result due to multiple comparisons.

Another potential limitation is the possible lower validity of the self-reported outcome. Although the validity of self-reported hypertension in the studied population is fair, the misclassification in the outcome could hide the studied associations. In fact, the correlation between self-reported and measured blood pressure was not very high. Similarly, the positive predictive value was only moderately good, due to false positive cases (i.e., those reporting hypertension but showing normal levels of blood pressure and not taking antihypertensive medication). The most likely explanation for these false positives is that the approach we used for the comparison (two measurements of blood pressure in the same day) is probably not good enough for a true "gold standard." Thus, our false positives are very likely those participants previously diagnosed with hypertension who had since undergone lifestyle changes that restored their blood pressure values to within normal limits. Interestingly, self-reported hypertension has been shown to result in enough accuracy in other epidemiological studies (12,13,22,23). We can assume that the same, if not better, validity can be applied to our population, given the higher educational level of our participants. Nevertheless, it could be probable that some degree of misclassification was associated with the exposure of interest, introducing an information bias. If olive oil consumption were associated with a lower awareness of hypertension, the observed beneficial relationship would be spurious. However, it has been previously reported that individuals in the SUN study following a Mediterranean diet, and therefore having higher olive oil consumption, had an overall healthier lifestyle and were more health-conscious (24). This fact suggests that the bias would go, in any case, in the opposite direction; that is, those with higher olive oil consumption would be more

aware of hypertension; thus the incidence of hypertension would be higher among them. This is contrary to our findings.

Finally, another potential problem is that dietary fat has a relatively quick turnover, and membranes and other cellular constituents might easily be affected after only a few weeks of feeding a diet different in FA composition (25). A short-term reduction in olive oil consumption is most likely to occur among people with a high baseline consumption of olive oil, because of regression to the mean. But that was not the case in our database, because a decrease in olive oil consumption was more likely (2.4%) among participants in the first quintile of baseline consumption than among those in the fourth and fifth quintiles (1.0 and 1.5%, respectively).

In conclusion, olive oil consumption seems to be associated with the incidence of hypertension among the highly educated males of our cohort, but we did not observe this association among women. With a longer follow-up period, it will be possible to confirm and strengthen the findings of this analysis. Olive oil appears to be a healthy food and a preferable substitute for other fats used for cooking.

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