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Carotid intima-media thickness is inversely associated with olive oil consumption

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Abstract

Background: Intima-media thickness (IMT) is a valid marker for generalized vascular disease whose main risk factors are associated with food habits and lifestyle. A Mediterranean food pattern may have a protective effect on cardiovascular mortality.
Objective: To assess the relationship between carotid IMT and olive oil consumption.
Methods: One hundred and ninety nine patients were randomly extracted from 1055 asymptomatic high cardiovascular risk participants at the AP-UNAV recruitment center of the PREDIMED (PREvención con DIeta MEDiterránea) project. Demographic and clinical variables were collected, and a validated semiquantitative food frequency questionnaire (137 items) was administered at the inclusion interview. A B-mode ultrasound imaging technique was used to measure the mean common carotid IMT.
Results: The mean age was 67.3 years and 53.3% were women. Energy-adjusted olive oil consumption quintiles were assessed as the main exposure after adjusting for potential dietary and non-dietary confounders. Using continuous carotid IMT as the outcome in an ANCOVA analysis, the adjusted IMT means throughout quintiles showed an inverse association with a plateau after the second quintile, with statistical differences when the adjusted IMT mean of the merged four upper quintiles were compared with the lowest quintile ($p < 0.05$). The averaged (both sides) mean IMT of the common carotid was dichotomised and values above the median (0.804 mm) were used to identify carotid atherosclerotic damage. We also found an inverse association of olive oil consumption with high IMT, throughout the second to the fifth quintile as compared with the lowest quintile. The adjusted OR was of 0.08 (95% confidence interval, CI, of 0.02–0.37; $p = 0.001$) after merging the four upper quintiles.
Conclusion: The inverse association between the olive oil consumption and the carotid IMT could suggest a protective role of olive oil against the development of carotid atherosclerosis in persons at high cardiovascular risk.

Keywords: Atherosclerosis; Cardiovascular risk; Mediterranean food pattern; Olive oil; Intima-media thickness

1. Introduction

Atherosclerosis is a diffuse inflammatory disease of the arterial wall, and it is the cause of a high number of fatal and non-fatal events worldwide. Atherosclerosis progresses unnoticed over years and several risk factors and markers of the disease have been the focus of attention for an early detection and prevention of its clinical end points [1,2].

Lifestyle appears to be the main trigger of a cascade of mechanisms leading to cardiovascular disease [3]. Food patterns and also a sedentary lifestyle are considered to be major determinants of cardiovascular risk factors and cardiovascular disease [4].

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Olive oil is the common main component of the Mediterranean food pattern. A high consumption of olive oil (i.e. the highest quintile, with a median intake of 54.3 g/day) has been found associated with protection from myocardial infarction in a case-control study [5], and dietary olive oil also was found to protect from total mortality in a cohort study of coronary patients in those who reported often or regularly consumption as compared with those reporting lower consumption (never or sometimes) [6]. Some studies have pointed out possible mechanistic explanations of this negative association of olive oil intake and cardiovascular disease, such as an improvement of endothelial function or an anti-inflammatory activity on the vessel wall [7,8].

Since arteriosclerosis may be silent for decades, some imaging techniques of the vascular wall previously validated in studies of cardiovascular risk can be considered as non-invasive end-points in epidemiological studies to evaluate the severity of atherosclerotic disease. Carotid intima-media thickness (IMT) measurements, acquired by means of B-mode ultrasound imaging, have been validated as surrogate markers in observational studies and experimental pharmacological trials [9]. Cardiovascular risk factors grouping determine a higher risk for more severe carotid arteriosclerosis as expressed by IMT, and also for increments of the percentage in subjects with significant carotidal lumen stenosis [10].

To date no studies have been published on the effect of olive oil or any composite food pattern on morphologic changes in the vascular wall, considered as the target of risk factors aggression. The PREDIMED (PREvención con DIeta MEDiterránea) study is a multicentre primary prevention trial evaluating major cardiovascular events as end points in asymptomatic patients with high risk for cardiovascular events [11]. To evaluate the influence of the baseline food habits on the carotid wall, a B-mode ultrasonographic measurement of IMT was done in a sample of the participants in one of the recruitment centers, before starting with them the intervention protocol. We analysed some possible associations between previous olive oil dietary consumption and the mean common carotid IMT as a marker of atherosclerosis.

2. Methods

The PREDIMED study is a large, parallel group, multicenter, controlled, and randomized, 4-year clinical trial aimed at assessing the effects of the Mediterranean diet on the primary prevention of cardiovascular disease (http://www.predimed.org). It has 10 recruitment centers in 8 Spanish cities. The trial protocol has been described elsewhere [11]. The AP-UNAV recruitment center, at Pamplona, is composed of seven health centers affiliated with the Department of Preventive Medicine and Public Health of the University of Navarra. From July 2003 to May 2005, 1055 high risk participants were recruited in our center after giving their written consent. Inclusion criteria were presence of diabetes mellitus, or three or more of the following risk factors: body mass index $\geq$25 kg/m^2, hypertension (blood pressure $\geq$140/90 mmHg or treatment with antihypertensive drugs), LDL cholesterol $\geq$160 mg/dl or treatment with lipid lowering drugs, HDL cholesterol $\leq$40 mg/dl, current smoking and family history of premature coronary disease. Exclusion criteria were: previous history of cardiovascular disease, any severe chronic illness, drug or alcohol addiction, history of allergy or intolerance to olive oil or nuts, and low predicted likelihood of changing dietary habits.

The initial evaluation consisted in the administration of a 137-item validated food frequency questionnaire [12], a validated physical activity questionnaire [13], and a 47-item questionnaire about educational, achievement, lifestyle, history of illnesses, and medication use. We performed anthropometrical, blood pressure and ankle–brachial index measurements, and obtained samples of fasting blood and spot urine.

The food frequency questionnaire was completed by a trained dietician in a face to face personal interview with each participant at the inclusion interview. They were asked for the frequency of consumption for each food item during the past year, specifying the usual portion size (semiquantitative assessment). Nine possibilities of frequency were offered from never to more than six times a day. Nutrient intakes were computed using Spanish food composition tables. All items were adjusted for total daily energy using the residuals method [14].

A random sample of 199 participants out the total 1055 patients (92% of acceptation) was extracted and, after a second written expression of consent, a B-mode ultrasound imaging of both carotids was performed.

IMT and atherosclerotic plaques of the carotid arteries were assessed by high-resolution B-mode ultrasound according to the standardized scanning protocols as previously described [15,16]. In brief, ultrasonography was performed with a 5–12-MHz linear-array transducer (ATL 1500 HDI). The left and right common carotid arteries were examined in anterolateral, posterolateral and mediolateral directions. Longitudinal images of the distal common carotid arteries in which the interfaces are most clear were obtained. IMT was measured in the far wall of the common carotid artery, 1 cm proximal to the carotid bulb in a region free of plaques with an optimum angle for measuring IMT at the proximal and distal wall. Plaque was defined as a localized echostructure that encroached into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or demonstrates a thickness of $\geq$1.5 mm beyond the interface between lumen and intima, according to Mannheim intima-media thickness consensus [17]. Subjects were examined by two certified sonographers blinded to all clinical and dietary information. Both sonographers were neurologist, with experience in ultrasound examination of the carotid artery, and they were specially trained in IMT measurements.

Measurements of IMT were performed offline using software developed for that purpose (M'Ath®, ICN-METRIS). The reader froze the best images of both common carotid arteries, including a minimum of 10 mm length of an arterial segment. IMT was automatically measured and the automated system provides the mean maximum value of more than 100 measurements performed on 10 mm.

The reproducibility of IMT measurements between and within sonographers had previously been reported [2]. The regression coefficient was 0.76 ($p < 0.0001$) and 0.82 ($p < 0.0001$), respectively [15].

Statistical analysis was done with SPSS 13.0. Differences in variables between quintiles were assessed with χ^2 and ANOVA for qualitative and quantitative variables, respectively. We used the residuals method to adjust olive oil consumption for total energy intake. The average common carotid IMT was calculated as the mean IMT measurement of both carotids. This variable was used as a continuous outcome for analysis of covariance (ANCOVA) to compare its adjusted means across quintiles of olive oil consumption. We also calculated the median IMT and its 95% confidence interval across quintiles of energy-adjusted olive oil consumption. We compared the median of the lowest against the median for the four upper quintiles using Mann–Whitney test. We also categorized the average common carotid IMT in two values using the median as the cut-off point. This new variable was also used as the outcome in multivariate non-conditional logistic regression modelling using quintiles of olive oil intake as the main exposure and adjusting for potential confounders. We adjusted all logistic models and ANCOVA models for known risk factors of atherosclerosis, including dietary and non-dietary potential confounders. Reported "*p*" values are two-tailed, and below 0.05 were considered statistically significant.

3. Results

The random sample consisted in 199 subjects, 53.3% women, with a mean age of 67.3 years (S.D.: 6.0 years).

The energy-adjusted olive oil consumption ranged from 6 to 74 g/day, and it was categorized in energy-adjusted quintiles to explore its association with the carotid IMT.

Table 1 displays the variables that might confound the association between olive oil consumption and carotid IMT. In the fifth quintile there were more participants with attained educational level higher than primary school, more married subjects, their average total energy intake was higher, and they also exhibited a higher intake of total fat and monounsaturated fatty acid consumption. However, the average intake of saturated and polyunsaturated fatty acids was similar across successive quintiles. A typical Mediterranean dietary pattern, with a high fat content (44% of total energy in the

Table 1
Distribution of potential confounders across energy-adjusted quintiles of olive oil consumption

Quintile	Q1	Q2	Q3	Q4	Q5	*p*
n	39	41	40	40	39	
Consumption (g/day)	6–34	35–41	42–45	46–53	54–74	
Age (mean (S.D.))	69 (6)	66 (6)	65 (5.5)	68.5 (5)	67 (6)	0.03
Women (%)	69	41	22	88	46	NS
Married (%)	56	65	85	67	85	NS
Primary educational level (%)	84	68	65	75	59	NS
Current smokers (%)	13	17	22	10	21	NS
Former smokers (%)	28	32	30	12	31	NS
Diabetes (%)	28	32	47	22	28	NS
Hypertension (%)	87	76	72	80	82	NS
Obesity (BMI > 30 kg/m^2) (%)	54	29	25	40	44	NS
Lipid lowering drugs (%)	49	44	55	30	41	NS
Anti-hypertensive drugs (%)	82	68	62	72	82	NS
Aspirin therapy (%)	28	19	27	20	20	NS
Body mass index (kg/m^2) (mean (S.D.))	30.7 (3.5)	28.5 (3.4)	29.1 (3.5)	29.6 (3.1)	29.1 (2.9)	NS
LDL cholesterol (mg/dl) (mean (S.D.))	137 (33)	133.1 (31.7)	124.4 (29.3)	149.6 (26.1)	126 (44.4)	0.04
HDL cholesterol (mg/dl) (mean (S.D.))	54.5 (14.6)	54.8 (13.1)	49.9 (10.6)	55.8 (12.6)	55.9 (13.0)	NS
Triglycerides (mg/dl) (mean (S.D.))	151.7 (70.8)	148.0 (82.2)	143.0 (67.5)	124.5 (43.1)	150.6 (70.9)	NS
Fasting blood glucose (g/dl) (mean (S.D.))	114.6 (33.5)	119.7 (41.2)	133.8 (40.8)	106.7 (43.7)	116.6 (29.2)	NS
Total energy intake (kcal/day) (mean (S.D.))	2125 (664)	2606 (621)	2239 (280)	2102 (198)	2420 (628)	0.001
Protein intake (%*E*) (mean (S.D.))	17 (3)	15 (3)	16 (2.5)	16 (2)	14 (2)	0.001
Carbohydrate intake (%*E*) (mean (S.D.))	44 (7)	41 (5)	37 (7)	39 (4)	38 (5)	0.001
Fat intake (%*E*) (mean (S.D.))	36 (6)	39 (5)	42 (5)	43 (4)	44 (5)	0.001
SFA intake (%*E*) (mean (S.D.))	10 (2)	10 (2)	10 (2.5)	10 (2)	10 (2)	NS
MUFA intake (%*E*) (mean (S.D.))	16 (2)	19 (2)	22 (2.5)	23 (2)	24 (3)	0.001
PUFA intake (%*E*) (mean (S.D.))	6 (3)	6.5 (3)	6.5 (2)	6 (1.5)	6 (1)	NS
Alcohol intake (g/day) (mean (S.D.))	9 (17)	20 (21)	17 (22)	5 (13)	13 (23)	0.008
Fiber intake (g/day) (mean (S.D.))	23 (7)	24 (7.5)	22 (6)	21 (4)	23 (6)	NS
Fruit consumption (g/day) (mean (S.D.))	345 (145)	308 (314)	314 (149)	320 (134)	323 (146)	NS
Vegetable consumption (g/day) (mean (S.D.))	270 (98)	257 (77)	296 (83)	250 (80)	290 (94)	NS
Nuts consumption (g/day) (mean (S.D.))	8 (12)	13 (12)	8 (10)	5 (13)	9 (13)	NS

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Table 2
Association between energy-adjusted quintiles of olive oil consumption and level of carotid atherosclerosis (IMT, mm)

	Q1	Q2	Q3	Q4	Q5
n	39	41	40	40	39
Consumption (g/day)	6–34	35–41	42–45	46–53	54–74
Median consumption	27	40	44	50	58
IMT Median (95% CI)	0.87 (0.80–0.94)	0.79 (0.76–0.85)	0.78 (0.76–0.84)	0.80 (0.74–0.88)	0.81 (0.77–0.86)
Adjusted IMT mean (95% CI)[a]	0.895 (0.840–0.951)	0.817 (0.764–0.870)	0.829 (0.770–0.887)	0.837 (0.776–0.899)	0.861 (0.803–0.918)
Adjusted IMT mean (95% CI)[b]	0.893 (0.838–0.947)	0.834 (0.800–0.868); $p = 0.04$			

Medians and adjusted means (95% confidence intervals) using ANCOVA; IMT: intimal-media thickness, mm. CI: confidence interval.
[a] Adjusted for age, gender, body mass index (continuous), total energy intake (continuous), glucose blood levels (continuous), LDL (continuous), HDL (continuous), high blood pressure (yes/no), and smoking (2 categories).
[b] Merging the four upper quintiles in a single category, multivariate adjustment as in (a).

fifth quintile) and high in monounsaturated fat (24% of total energy in the fifth quintile) was found in most of our participants. The dietary pattern also reflected a high fiber, fruit, vegetable and nuts intake for all quintiles of olive oil consumption.

The average IMT values interval was from 0.46 to 1.56 mm, with a mean of 0.84 (S.D.: 0.15 mm).

We assessed the association between olive oil consumption and IMT comparing the median IMT and their 95% confidence intervals across quintiles of energy-adjusted olive oil consumption. The highest median was observed for those with the lowest consumption of olive oil (Table 2). When we compared the IMT median for the lowest quintile of olive oil consumption (0.87 mm) versus the median of the merged four upper quintiles (0.79 mm) the result was marginally significant ($p = 0.07$).

We found the results shown in Table 2 using as the outcome carotid IMT as a continuous variable (ANCOVA). These results suggested a non-linear inverse association between energy adjusted-olive oil consumption and carotid IMT with a plateau after the second quintile. We observed the lowest adjusted IMT means for the 2nd and 3rd quintiles of consumption. The inverse association was apparent when we merged the second to the fifth quintile and compared them against the lowest quintile suggesting a significant reduction ($p < 0.05$) in average carotid IMT value associated with olive oil intakes higher than 34 g a day.

The overall median for IMT (0.804 mm) was used as the cut-off point to dichotomise the ITM variable below and above that value into two groups of equal size. This new variable, indicating a category of patients with higher IMT readings was used as the dependent variable in the logistic regression models.

To explore a possible association between dietary energy adjusted-olive oil and the carotid IMT, several logistic regression analyses were run. First a multivariate logistic regression was adjusted for age and sex. A second model was additionally adjusted for body mass index, plasma glucose, LDL cholesterol, HDL cholesterol, and presence of diabetes, hypertension, and smoking in three categories (never, former, current). Lastly the model was also adjusted for dietary confounders (total energy, saturated fat, fiber, cholesterol, and alcohol intake). The more striking finding was a significant effect throughout the second to the fifth quintile, suggesting a threshold in the negative association between the consumption of olive oil and higher carotid IMT. Merging the last four quintiles the OR was 0.08 (95% confidence interval, CI: 0.02–0.37; $p = 0.001$), indicating a highly significant negative association with a presumed marker of vascular damage (IMT above the median) for intakes of olive oil higher

Table 3
Association between energy-adjusted quintiles of olive oil consumption and the risk of carotid atherosclerosis (IMT above median)

Quintile	Q1	Q2	Q3	Q4	Q5
n	39	41	40	40	39
High/low IMT	24/15	18/23	16/24	19/21	20/19
Consumption (g/day)	6–34	35–41	42–45	46–53	54–74
Median	27	40	44	50	58
Unadjusted	1 (ref.)	0.28 (0.10–0.83); $p = 0.02$	0.28 (0.10–0.83); $p = 0.02$	0.33 (0.11–1.00); $p = 0.05$	0.52 (0.18–1.53); $p = \text{NS}$
Sex- and age-adjusted	1 (ref.)	0.21 (0.07–0.68); $p = 0.009$	0.17 (0.05–0.57); $p = 0.004$	0.40 (0.12–1.13); $p = \text{NS}$	0.45 (0.14–1.46); $p = \text{NS}$
Multivariate adjusted[a]	1 (ref.)	0.23 (0.07–0.82); $p = 0.02$	0.15 (0.04–0.62); $p = 0.009$	0.45 (0.13–1.55); $p = \text{NS}$	0.43 (0.12–1.54); $p = \text{NS}$
Multivariate adjusted[b]	1 (ref.)	0.07 (0.01–0.36); $p = 0.001$	0.07 (0.01–0.45); $p = 0.005$	0.14 (0.02–0.83); $p = 0.03$	0.12 (0.02–0.90); $p = 0.04$
Multivariate adjusted[c]	1 (ref.)	0.08 (0.02–0.37); $p = 0.001$			

Unconditional logistic regression models. Odds ratios (95% confidence intervals); IMT: intimal-media thickness.
[a] Additionally adjusted for body mass index (continuous), diabetes (yes/no), glucose blood levels (continuous), LDL-cholesterol (continuous), HDL-cholesterol (continuous), high blood pressure (yes/no), and smoking (never/former/current).
[b] Additionally adjusted for the variables used in (a) plus total energy intake, carbohydrate intake, saturated fat intake, fiber intake, dietary cholesterol and alcohol consumption.
[c] Merging the four upper quintiles in a single category, multivariate adjustment as in (b).

than 34 g a day after adjusting for potential confounders (Table 3).

Analysing separately both sexes with a multivariate-adjusted non-conditional logistic regression, fitted as previously, a negative association for the merged four upper quintiles with respect to the first quintile was found only in the group of women ($n = 106$), with an OR of 0.30 (95% CI: 0.00–0.31, $p = 0.004$), while in the group of men ($n = 93$) the OR was of 0.12 (95% CI: 0.01–1.34, non-significant). However, in the ANCOVA analysis no interaction was observed between sex and energy adjusted olive oil consumption for the effect on the carotid wall.

4. Discussion

Several reports of cardiovascular risk have used carotid IMT as an end point. This marker has been consistently associated with coronary disease incidence, stroke incidence and it also allows the prediction of peripheral artery disease (intermittent claudication). These findings are consistent in several cohorts, such as the Cardiovascular Health Study [18], The Rotterdam study [19], and the Atherosclerosis Risk in Communities (ARIC) [20]. That association implies the concept of generalized vascular damage associated with higher values of carotid IMT. The differences in the risk of clinical events have been reported to be significant among quintiles of IMT [18], and also when IMT was used as a continuous variable. An increment of 0.2 mm in carotid IMT has been reported to imply a 28% and a 31% increment of risk for stroke and myocardial infarction, respectively [9].

Reduction of carotid IMT was the objective of some trials using statins. These trials have demonstrated a significant effect of pharmacological interventions both in asymptomatic subjects and in patients with coronary disease, with a wide range of plasma cholesterol values [21,22]. The decrease of IMT carotid arteries observed after treatment accounts for a favourable impact in cardiovascular events. These facts are the main basis for other studies searching for causal mechanisms of atherosclerosis itself using IMT as the outcome.

Regardless of the presence of predisposing factors for a variety of diseases, food habits have a direct influence in morbidity and mortality during the course of life, as WHO has stated in several reports. In a recent epidemiologic study (the EPIC-Greece), an index for adherence to a Mediterranean food pattern was associated with a reduction in total and cardiovascular mortality [23]. Similar results were reported in the HALE cohort, among older people from several European countries [24]. However, a decrease in the incidence of clinical non-fatal cardiovascular events was not demonstrated.

The present paper associates a higher dietary consumption of an outstanding Mediterranean food, as it is olive oil, with the presence of lower values of carotid IMT. The B-ultrasound reading for IMT in normal people changes with age and reaches a value of 0.77 in seniors citizens [9]. There is not an established cut-off point for this parameter at present. In a study performed at Barcelona, Spain, the 75th percentile of carotid IMT for subject older than 65 years was 0.89 mm for men and 0.82 mm for women [25]. We used the median of the average carotid IMT in our sample (0.804 mm) to split the sample into two groups of equal size (lower than median and higher than median IMT values). A dichotomization of the IMT variable was previously used in the ARIC study [20]. They compared extreme values with not extreme (higher or lower than 1 mm) to assess the risk for coronary heart disease incidence. The cut-off value used in this study is only valid in terms of comparison between groups, and we used the median to avoid arbitrary categories. At this moment no threshold for carotid IMT has been reported as a valid cut-off to define pathological vascular thickening.

However, we used an ANCOVA as the first and major analysis considering the average IMT as the outcome. The negative association between high IMT values and olive oil found in the adjusted ANCOVA, after accounting for possible confounders is coherent with the logistic regression results, showing that higher olive oil consumption is associated in our sample with significant decreases in the average value of IMT in a non-linear manner. Taking together both analyses, a protective role of olive oil on the vascular wall could be suggested. The finding of negative estimates of similar magnitude throughout the second to the fifth quintile when comparing them with the first quintile deserves some explanation. The levels of consumption of olive oil found in our participants are higher than expected. In other studies performed in similar settings the median of the second quintile was 12 g/day, clearly lower than the median of the same quintile in our participants (40 g/day) [5]. This may be explained because of the very likely previous medical advice issued to these high-risk participants to follow a protective diet such as the Mediterranean food pattern, usually considered healthy in Spain. This explanation is plausible because all included patients in our study belong to a category of high cardiovascular risk and are under periodical follow-up in their health centers. However, this possible change in dietary pattern is always previous to the inclusion in the study and constitutes the habitual diet evaluated with the food frequency questionnaire at the inclusion interview. Consequently, the possible change in food pattern has not been induced by recent advice.

In a previous study with a case-control design, quintiles of energy-adjusted olive oil consumption showed a progressive protection for a first myocardial infarction. But in that study the olive oil consumption was progressively increasing from the first quintile (median of 7.2 g/day) to the highest (median of 54.3 g/day). In this study on the effect of energy-adjusted olive oil consumption on carotid IMT in high risk patients, we are comparing the effect of 58 g/day of olive oil (median of the fifth quintile) with 27 g/day (median of the first quintile), with scarce differences in the consumption of olive oil from the second to the fifth quintiles. Probably this is the explanation

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of the apparent threshold effect instead of a progressive effect of the olive oil on the carotid wall. Also it may explain a lack of clear differences between quintiles except when the four upper quintiles are merged as a category.

Oleic acid, the main monounsaturated fatty acid in the olive oil, added to cultured endothelial cells induced a decrease in vascular cell adhesion molecule-1 expression and in the transcription of its messenger RNA, and a diminished adherence of a monocyte cell line [8,26]. A randomized study showed that a monounsaturated fatty acid rich diet, similar to the Mediterranean diet, increased the endothelium dependent vasodilatation with respect to National Cholesterol Education Program type diet [7].

In unstable angina patients olive oil consumption and an index of Mediterranean diet adherence were associated to lower values of vascular cell adhesion molecule-1 and tumor necrosis factor-alpha in the coronary sinus blood [27]. Therefore, olive oil might induce protection against inflammatory phenomena in the coronary wall, which could also explain the lower IMT in the carotidal wall found in this report.

The main limitation of this research is the small number of subjects examined. The carotid ultrasound was not a part of the initial exam of all the participants included in the PREDIMED study. As all of them are high risk patients we assumed a high proportion of patients would have objective vascular damage. The final estimates are striking and the wide range of confidence intervals can be attributed to the limited sample size. Nevertheless, the significance of the negative association in the logistic regression and the marginal statistical significance in the linear regression model allow us to suggest a protective effect of olive oil on the progression of the systemic atherosclerosis.

These results need a confirmatory research. The first question is whether olive oil will be able to reduce high IMT in people with regular consumption of it. The second question is for how long this exposure to olive oil would be necessary to be maintained to observe that effect. The suggestion of this paper has been drawn from subjects with high olive oil consumption for years. Is the effect a matter of long-term exposure to a high consumption or is the exposition to olive oil suitable to be used as a short-term intervention to reduce arterial wall atherosclerotic damage? In the PREDIMED study and in other ongoing studies some of these questions could be answered.

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