Clin. Cardiol. 30, 125–129 (2007)

The Impact of Olive Oil Consumption Pattern on the Risk of Acute Coronary Syndromes: The Cardio2000 Case–Control Study.

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Summary

Background: According to epidemiological and metabolic studies monounsaturated fatty acids (MUFAs) seem to exert a protection against coronary heart disease (CHD) risk. The aim of the present study was to evaluate the association between the pattern of edible oils and fats consumption and the prevalence of a first, nonfatal event of an acute coronary syndrome (ACS) in a Greek sample.

Methods: Seven hundred males and 148 females patients with first event of an ACS and 1078 population-based controls, age and sex matched, were randomly selected. Detailed information regarding their medical records, alcohol intake, physical activity and smoking habits was recorded. Nutritional habits were evaluated with a semi-quantitative food-frequency questionnaire and use of oils in daily cooking or preparation of food was also recorded. Multiple logistic regression analysis estimated the odds ratio (OR) of having ACS by types of oil used, after taking into account the effect of several confounders.

Results: Exclusive use of olive oil was associated with 47% (95% confidence interval (CI) 0.4–0.71) lower likelihood of having ACS, compared to nonuse, after adjusting for BMI, smoking, physical activity level, educational status, the presence of family history of CHD, as well as hypertension, hypercholesterolemia and diabetes. Consumption of olive oil in combination with other oils or fats was not significantly associated with lower odds of ACS compared to no olive oil consumption ($p = 0.14$).

Conclusions: Exclusive use of olive oil during food preparation seems to offer significant protection against CHD, irrespective of various clinical, lifestyle and other characteristics of the participants.

Key words: olive oil, acute coronary syndromes, myocardial infarction

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Introduction

The role of dietary lipids in the etiology of coronary heart disease (CHD) continues to evolve as we gain a better understanding of the metabolic effects of individual fatty acids and their impact on surrogate markers of risk. Saturated fatty acids have been associated with a higher risk of CHD, whereas monounsaturated fatty acids (MUFAs) and n-3 polyunsaturated fatty acids have protective effects against CHD.[1]

One of the most important characteristic of the Mediterranean diet is the presence of virgin olive oil as the principal source of energy from fat, which is a good source of MUFA and hundreds of micronutrients.[2] The seven countries study yielded the first convincing epidemiologic evidence for a negative correlation between the dietary intake of MUFA and mortality from CHD.[3] Moreover, regression analysis of data of the Nurses Health study confirmed a protective effect of MUFA with regard to CHD risk.[4]

A protective role for olive oil on mortality among patients with a previous myocardial infarction (MI) has

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Received: July 26, 2006
Accepted with revision: October 16, 2006

Published online in Wiley InterScience
(www.interscience.wiley.com).
DOI:10.1002/clc.20043

been found in the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto miocardico (GISSI)- Prevenzione trial,[5] while case–control studies have shown conflicting results, indicating no association[6,7] or inverse association[8] between olive oil and risk of CHD. A Greek case–control study[9] focused on the type of cooking oil, reported no significant protection from MUFA intake against CHD, while investigators from the EPIC study showed that olive oil intake, per se, was inversely associated with both systolic and diastolic blood pressure, surrogate markers of CHD.[10]

The aim of the present study was to evaluate the association between the pattern of olive oil and other oils and fats consumption in daily cooking or preparation of food and the prevalence of a first, nonfatal event of an acute coronary syndrome (ACS) (MI or unstable angina [UA]), in a Greek sample.

Materials and Methods

Patients and Controls

The CARDIO2000 is a multicenter case–control study that explores the association between several sociodemographic, nutritional, lifestyle and clinical factors with the risk of developing nonfatal ACS. In the study participated 848 out of 956 patients, randomly preselected from the hospitals, with a first symptom of CHD in their life. The number of participants was determined through power analysis, in order to evaluate a minimum difference of 7% in odds ratios (OR) per one unit increase in the explanatory variables (statistical power 0.80, p-value <0.05). The inclusion criteria for the patients were as follows:

1. first event of acute MI diagnosed by two or more of the following features: typical electrocardiographic changes, compatible clinical symptoms, specific diagnostic enzyme elevations, or
2. first diagnosed UA corresponding to class III of the Braunwald classification.[11]

We also randomly selected 1,078 subjects (830 males and 248 females) without any clinical symptoms or suspicious of cardiovascular disease, in their medical history (controls), matched to the patients by age (± 3 years), sex, and region.

Exposure Parameters

Information regarding medical factors was retrieved from medical records and lifestyle characteristics information through a detailed questionnaire. Nutritional habits were evaluated with a semiquantitative food-frequency questionnaire.[12] In addition, consumption of olive oil, vegetable seed oils, butter and margarines was assessed, by asking all participants about the use of oils in daily cooking and/ or preparation of food (e.g. addition to salads, etc.). Data concerning alcohol consumption, smoking status, physical activity and education level, as well as the presence of premature CHD among first-degree relatives, weight and height, were also recorded.

Hypertension was defined as systolic/diastolic blood pressure $>140/90$ mmHg or use of special treatment, hypercholesterolemia as total cholesterol >200 mg/dl or use of lipid-lowering agents and diabetes as fasting blood glucose >125 mg/dl or use of antidiabetic medication.

The CARDIO2000 study was approved by the Ethics Committee of the Department of Cardiology, Athens Medical School. Further details regarding the (CARDIO2000) study have been previously presented.[13]

Statistical Analysis

Continuous variables are presented as mean $\pm$ standard deviation, while categorical variables as absolute and relative frequencies (%). Contingency tables with calculation of chi-squared test evaluated associations between the categorical variables. Using Student's t-test, we evaluated the associations between groups of study and normally distributed continuous variables. Logistic regression analysis was performed for calculating OR of having ACS and their corresponding 95% confidence intervals (CIs). According to oil usage, subjects were categorized into three groups. All the interactions between the exposure variables and the main factor of interest were evaluated, as well as potential confounding effect of the other exposure variables. All reported p-values are two-sided and compared to a significant level of 5%. STATA 8 software was used for the calculations (STATA Corp. College Station, Chicago, IL, USA).

Results

Exclusive use of olive oil was reported by 65.2% of controls and 58.6% of patients ($p = 0.002$), whereas no use of olive oil was reported by 16.3% of controls and 22.4% of patients ($p = 0.002$). Olive oil plus other oils or fats consumed 18.5% of the controls and 19% of patients ($p = 0.002$).

Table 1 presents various characteristics of the patients and controls, by the pattern of oil consumption. Particularly, among patients, no significant associations between oil consumption pattern and several demographic and clinical characteristics were observed. However, in controls, oil consumption pattern was associated with age, sex, body mass index (BMI), smoking, prevalence of hypertension and hypercholesterolemia and these factors were taken into account during the regression analysis. Moreover, in both patients and controls, we observed that those who used olive oil had lower consumption of white meat ($p < 0.001$) and higher consumption of fish

TABLE 1 Demographic and clinical characteristics of the participants

	Type of oil			
	No use of olive oil	Exclusive use of olive oil	Olive plus other oils/ fats	p^+
Patients, n	190	497	161	
Age	62 ± 11	61 ± 9	59 ± 10	0.08
Male, (%)	83	84	78	0.22
Higher education (%)	9	14	20	0.27
Sedentary life (%)	83	75	76	0.64
Body mass index (kg/m^2)	27 ± 2	27 ± 4	28 ± 4	0.49
Current smoking (%)	63	67	70	0.44
Hypertension (%)	45	48	51	0.55
Hypercholesterolemia (%)	54	61	65	0.11
Diabetes Mellitus (%)	28	26	23	0.57
Family history of cardiovascular disease (%)	46	45	42	0.7
Controls, n	176	702	198	
Age	56 ± 12	62 ± 10	58 ± 11	<0.001
Male, (%)	75	64	75	0.002
Higher education (%)	17	20	22	0.01
Sedentary life, %	83	79	80	0.84
Body mass index (kg/m^2)	28 ± 4	27 ± 4	26 ± 3	<0.001
Current smoking, %	56	46	58	0.002
Hypertension, %	25	31	21	0.018
Hypercholesterolemia, %	19	35	14	<0.001
Diabetes mellitus, %	11	9	9	0.77
Family history of cardiovascular disease (%)	14	18	14	0.36

$^+$ p-values derived from ANOVA or chi-square test.

($p < 0.001$), legumes ($p = 0.002$), fruits and vegetables ($p < 0.001$), compared to nonolive consumers.

The age and sex adjusted OR of having ACS was 0.66 (95% CI 0.52 to 0.84) for those consuming olive oil exclusively, compared to those not using olive oil, whereas consumption of both olive oil and other oils/ fats did not show any significant relationship. However, it should be mentioned that the latter subgroup had smaller sample size and this affect the statistical power to detect a difference (i.e. statistical power = 67% for OR equal to 0.77 with the specific sample size). When we also adjusted for BMI, smoking, physical activity level, educational status, the presence of family history of CHD, as well as hypertension, hypercholesterolemia and diabetes, multiple logistic regression analysis revealed that the exclusive use of olive oil was associated with 47% lower likelihood of having ACS (95% CI 0.4 to 0.71), after controlling for factors mentioned above. It should be also mentioned that consumption of olive oil in combination with other oils/ fats was not significantly associated with lower odds of ACS compared to no olive oil consumption ($p = 0.14$). The association between olive oil intake and likelihood of ACS was not altered when we also adjusted for the consumption of various food groups or alcohol (Table 2).

Finally, residual confounding may still exist, thus we stratified our analysis by hypercholesterolemia, diabetes and hypertension status. We found that in people who had hypercholesterolemia before the acute cardiac event, exclusive olive oil consumption was associated with 0.55 times lower likelihood of having ACS (95% CI 0.35 to 0.81), while when diabetes status was taken into account no significant associations were observed. Finally, when we stratified our analysis by hypertension status we observed that exclusive olive oil consumption was associated with 48% lower likelihood of ACS (OR = 0.52, 95% CI 0.34 to 0.81) among hypertensive subjects, as well as among people who had normal blood pressure levels (OR = 0.59, 95% CI 0.42 to 0.85). No other significant interactions were observed between pattern of olive oil intake and various socio-demographic, lifestyle or other clinical characteristics and the likelihood of having ACS.

Discussion

The present study revealed that exclusive use of olive oil during cooking and as added oil is significantly associated with lower odds of having acute coronary events, even after controlling for several potential confounding risk factors.

Greece is a country that traditionally uses olive oil during the preparation of food. In the EPIC study the highest olive oil consumption was reported in Greece[14] and according to the Data Food Networking (DAFNE)

TABLE 2 Odds ratios (95% confidence interval) for nonfatal acute coronary syndromes associated with pattern of olive oil consumption

	Odds ratio	95% confidence interval		P
Oil category				
No use of olive oil (reference category)	1.00	-	-	
Exclusive use of olive oil	0.53	0.34	0.71	<0.001
Olive plus other oils or fats	0.77	0.54	1.09	0.14
Age (per year)	1.03	1.01	1.04	<0.001
Male vs. female sex	2.73	2.10	3.63	<0.001
Family history of cardiovascular disease (yes vs. no)	4.07	3.20	5.19	<0.001
Current smoking habits (yes vs. no)	1.79	1.41	2.27	<0.001
Hypertension (yes vs. no)	1.94	1.54	2.45	<0.001
Hypercholesterolemia (yes vs. no)	3.76	3.01	4.69	<0.001
Diabetes mellitus (yes vs. no)	2.39	1.76	3.25	<0.001
Body mass index (per 1 kg/m^2)	0.97	0.94	1.00	0.07
Physical inactivity (yes vs. no)	0.81	0.65	1.00	0.05
Higher vs. medium or lower education	0.94	0.70	1.20	0.68
Red meat intake (servings/week)	1.68	1.40	2.03	<0.001
Fruits and vegetables intake (servings/week)	0.66	0.57	0.76	0.001
Cereals intake (servings/week)	1.15	0.98	1.33	0.06
Alcohol intake (wineglasses/day)	1.09	0.97	1.22	0.14

project, Mediterranean countries had the least availability of added animal and vegetable fat and olive oil was the primary vegetable oil available in Greece and Spain.[15] In the present study 65% of controls and 59% of patients reported exclusive use of olive oil, whereas no use of olive oil was reported only by 16% of controls and 22% of patients. Moreover, people who reported exclusive use of olive oil also reported higher consumption of fish, legumes, fruits and vegetables, reflecting a dietary pattern close to the Mediterranean diet. However, the olive oil effect on the reduction of CHD risk was independent of these food groups.

An inverse association between olive oil consumption and the risk of AMI was also found in a case–control study from Spain[8] in which the upper quintile of energy adjusted olive oil was associated with a statistically significant 82% relative reduction in the risk of AMI, after adjustment for several confounders. Unfortunately, our data did not allow us neither to quantify the oils and fats intake nor to estimate the amount of MUFA consumed, however, the recording of type of added oils and fats during food preparation (i.e. cooking, frying, salad dressing) could include less recall bias than a quantitative approach and gave us important information that allow messages for public health to be carried out.

The observed unique effect that olive oil use seems to exert on CHD risk can be attributed to several effects of olive oil, e.g. in the reduction of total and LDL cholesterol and triglycerides levels.[16–18] In addition, a diet rich in olive oil reduces the thrombotic propensity[19] and may slow the development of coronary atherosclerosis.[20] MUFA also exert a protective effect against LDL oxidation[20] and oleic acid appears to interfere directly with the inflammatory response that characterizes early atherogenesis.[21]

In the hypercholesterolemic subjects of our sample exclusive olive oil consumption was associated with 0.55 times likelihood of ACS and this is in line with the results of several metabolic studies.[16,17] Additionally, the third report of the national cholesterol education program (NCEP) Adult Treatment Panel[22] recommended a program of therapeutic lifestyle changes that emphasized more on fat quality, promoting the ingestion of MUFAs, than on the quantity of dietary fat. Although metabolic studies have shown that olive oil improves lipid profile and glycemic control in diabetic patients,[23] we failed to show any significant association in this group of patients, probably due to the small number of diabetic people included in our sample. Finally, we observed that exclusive olive oil consumption was associated with 48% lower likelihood of ACS among hypertensive subjects. Olive oil has been inversely associated with blood pressure in epidemiological studies[10] and has been shown to lower blood pressure and reduce daily antihypertensive dosage among hypertensives.[24]

Limitations

In case–control studies two, main, sources of systematic errors may exist, the selection and the recall bias. In order to eliminate selection bias we tried to set objective criteria, both, for patients and controls. However, insignificant misclassification may exist, since a small percentage of asymptomatic coronary patients may be wrongly assigned to controls, even if they were evaluated by a cardiologist. Concerning information bias we tried to avoid it through accurate and detailed data from the subjects' medical records. Moreover, the coronary patients who died at entry or the day after were not

included into the study. This bias could influence our results, but, since this proportion of deaths was estimated between 2 and 4%, we believe, that it did not alter our findings significantly. Furthermore, regarding the potential effect of uncontrolled—unknown confounders, we tried to reduce it by using the same study base, both, for patients and controls.

Conclusions

According to our findings, exclusive use of olive oil during cooking and food preparation is significantly associated with 47% lower likelihood of having ACS and should be promoted through cardiovascular disease prevention programmes.

Acknowledgements

The authors would like to thank the physicians that coordinated the data collection: K Tzioumis (Athens, Crete, Pelloponisos), J Skoumas (Athens), N Papaioannou (Athens, Thessalia), P Stravopodis (Ionian Islands), L Karra (Aegean Islands), D Antoniades (Macedonia), G Rembelos (Aegean Islands), D Markou (Athens), A Moraiti (Athens), D Evagelou (Crete), S Vellas (Attica, Hpeirous), G Skoumbourdis (Sterea Hellas), B Meidanis (Macedonia, Sterea Hellas, Thessalia), S Loggos (Attica), I Elefsiniotis (Athens), N Marinakis (Aegean Islands), G Koutsimbanis (Thrace) and S Zombolos (Peloponnese).

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