Effects of canola or olive oil on plasma lipids, lipoprotein-associated phospholipase A2 and inflammatory cytokines in patients referred to coronary angiography

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Research

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Abstract

Background: The potential cardioprotective benefits of olive oil (OO) and canola oil (CO) consumption have been shown in some studies. The present study was conducted to compare the effects of CO and OO on plasma lipids, some inflammatory cytokines, and lipoprotein-associated phospholipase A2 (Lp-PLA2) mass and activity in patients undergoing coronary angiography.

Methods: A randomized, controlled, parallel-arm, clinical trial involving 48 patients (44 men and 4 women, aged 57.63 ± 6.34 years) with at least one classic cardiovascular risk factor (hypertension, dyslipidemia, or diabetes) who referred to coronary angiography was performed. Patients were randomly divided into two groups and received 25 mL/day refined olive oil (n=24) or canola oil (n=24) for 6 weeks. Plasma lipids, some selected inflammatory markers, and Lp-PLA2 levels were measured at the baseline and after the intervention.

Results: CO consumption produced a significant reduction in plasma Lp-PLA2 mass (-0.97 ± 1.84 vs 0.34 ± 1.57 ng/mL, p = 0.008 for CO and OO, respectively), whereas the mean changes of IL-6 concentration were significantly lower after OO consumption compared with CO (-9.46 ± 9.46 vs -0.90 ± 6.80 pg/mL, p = 0.008 for OO and CO, respectively). After 6 weeks of intervention, no significant changes were observed in plasma Lp-PLA2 activity, complement C3, C4, and lipid profile in two intervention groups.

Conclusions: Daily consumption of either of the refined olive or canola oils during a relatively short time could improve one of the inflammatory CVD risk factors.

Trial registration: IRCT20160702028742N5 at www.irct.ir (04/19/2019)

Background

Reducing the amount of dietary saturated fatty acids (SFAs) and replacing them with unsaturated fats are among the main nutritional recommendations for the prevention and treatment of cardiovascular disease (CVD) [1]. Inclusion of vegetable oils rich in monounsaturated fatty acids (MUFAs) in the diet has been associated with several cardioprotective effects [2]. Olive and canola oils that are two commonly consumed vegetable oils are low in SFAs and rich in MUFAs could be included in the context of a healthy diet for cardioprotection [3, 4]. The potential cardioprotective benefits of olive oil (OO) consumption, especially in the context of the Mediterranean diet, have been extensively studied [3, 5]. However, scientific evidence supports that replacing SFAs with polyunsaturated fatty acids (PUFAs) from vegetable oils reduces CVD somewhat more than with MUFAs [1]. Therefore, oils with low SFAs that contain a relatively high PUFAs, as well as high levels of MUFAs may be preferable to improve cardiovascular risk factors. Canola oil (CO) which contain low amounts of SFAs, high MUFAs and relatively high PUFAs could be a reasonable choice to be included in the healthy diet to replace SFAs and increase unsaturated fats intake [6], and evidence supports several potential health benefits of canola oil consumption in terms of reducing cardiovascular risk factors and improving health. [4]. In comparison between canola and olive oils, the MUFA content of OO is slightly higher, while the amount of PUFA is higher in CO [4]. In addition to

the classic CVD risk factors such as plasma lipid and lipoprotein concentrations, measuring inflammatory biomarkers is useful for cardiovascular risk assessment and predicting cardiovascular risk [7, 8]. Numerous inflammatory biomarkers are implicated in atherosclerosis, each one increases our understanding of this complex process. Interleukin-6 (IL-6) is among the well-studied inflammatory biomarkers related to cardiovascular risk [8-11]. Lipoprotein-associated phospholipase A2 (Lp-PLA2) is a member of the phospholipase A2 family that is produced by inflammatory cells and mediates vascular inflammation [12]. Elevated plasma Lp-PLA2 activity is positively correlated with an increase in inflammatory cytokines particularly IL-6 [13]. A meta-analysis of the prospective studies of Lp-PLA2 showed an association of both Lp-PLA2 activity and mass with a worse prognosis of coronary artery disease (CAD), ischemic stroke, and vascular mortality [14]. In particular, a higher level of Lp-PLA2 activity may imply a worse cardiovascular prognosis in high-risk patients referred to coronary angiography [15]. In addition to the effects that fatty acids intake can have on the concentration of lipids and inflammatory markers, they may affect the concentration of plasma C3 [12] which is itself have been associated with atherosclerosis and cardiovascular risk factors [16]. Research comparing the impact of olive and canola oils on cardiovascular biomarkers, particularly on inflammatory biomarkers is scarce. Therefore, the present study was performed aiming to compare the effects of CO and OO on plasma lipids, inflammatory cytokines, Lp-PLA2 mass and activity, and complement C3 and C4 concentrations in individuals undergoing coronary angiography.

Materials And Methods

Participants

The participants were patients who referred to coronary angiography in the Shahid Rajaei Cardiovascular, Medical & Research Center in Tehran, Iran. Eligible subjects were men and post-menopausal women less than 75 years who had at least one of the major cardiovascular risk factors including hypertension, diabetes mellitus, dyslipidemia, or acute cardiac events. None of the subjects had taken anti-inflammatory medication or dietary antioxidants or omega-3 supplements during the previous month before the study. Participants with low adherence to the intervention (who consumed less than 80% of the olive or canola oils delivered at the baseline), any changes in the disease treatment plan including type or dose of medications or coronary artery bypass graft (CABG) and gastrointestinal complications such as diarrhea were excluded from the study.

Study Design

The present study was a randomized, controlled, parallel-arm, clinical trial that was conducted in the spring and summer 2019 in Tehran, Iran. At baseline, demographic and medical information were obtained through face-to-face interviews and study of medical files, respectively. Next, the participants were randomly assigned to one of the two groups following simple randomization procedures using computerized random numbers and were requested to consume a daily amount of 25 mL of refined olive oil (OO) (Etka, Iran) or canola oil (CO) (CanaPlus, Canada) as raw with meals for 6 weeks. Olive and

canola oils were provided to patients in sufficient quantities. To ensure compliance with the intervention and proper oil consumption, participants were followed up weekly by telephone contact.

The procedures followed in this trial were in accordance with the 1964 Helsinki Declaration and the study protocol was approved by the Ethical Committee of National Nutrition & Food Technology Research Institute, Tehran, Iran (The ethical committee No. IR.SBMU.NNFTRI.REC.1398.074) and written informed consent were obtained from all the participants. This clinical trial was registered at the Iranian Registry Center of Clinical Trials (IRCT) (registration number: 20160702028742N5).

Anthropometric measures

Weight and height were measured at the baseline and after 6 weeks of intervention by the study dietitian. Weight was measured without shoes, coats, or jackets using a digital scale. Height was measured without shoes using a wall-mounted stadiometer.

Biochemical parameters

Venous blood samples were obtained from each patient after 12-hr overnight fasting and collected into heparinized tubes at baseline and after 6 weeks. The blood samples were centrifuged (4000 rpm for 20 min) and the resulting plasma was stored at -80°C. Plasma Lp-PLA_2 mass and activity were analyzed by a commercially available ELISA kit (ZellBio, Germany) and commercial colorimetric assay kit (Cayman Chemical Co.), respectively. Commercially available ELISA kit (BioLegend, USA) was used to measure plasma IL-6 concentration. Plasma complement C3 and C4 were determined by the *turbidimetric* method and lipid profile by the colorimetric method by commercial kits (Pars Azmoon, Iran) using an auto-analyzer (Selectra 2, Vital Scientific, Spankeren, The Netherlands).

Dietary intakes and physical activity

Dietary intake and physical activity levels were monitored at baseline and after 6 weeks. Dietary intakes were assessed using the 24-hr dietary recall questionnaire completed in three days (two regular days in the middle of the week and one day at the weekend) by the trained dietitian. Participants were asked to maintain their habitual lifestyle throughout the study. Recall data was analyzed using the Nutritionist software (version IV, N-Squared Computing, San Bruno, CA, USA) to which was added the local food data.

Statistical analysis

Although our primary outcome was Lp-PLA_2, we could not calculate sample size based on this variable because according to our search, there was no study comparing the effects of CO and OO on Lp-PLA_2 mass or activity. On the other hand, studies have shown that Lp-PLA_2 is transported in plasma predominantly (80%) is associated with LDL-C [17]. Therefore, the study sample size was calculated using LDL-C as the main outcome variable. To detect a change in the mean of LDL-C concentration (10 mg/dL) as reported in a previous investigation [18] at the 5% level of significance and with 80% power, 24 participants were needed in each arm of the two-arm trial.

The data were analyzed using the SPSS software for Windows version 21 (SPSS Inc., Chicago, IL, USA). All values were reported as Mean ± SD or percentage (%). The per-protocol analysis was performed (i.e. only those who completed the study were included in the analyses). The normality of distribution of the study variables was tested by the Shapiro-Wilk test. When the variables were not normally distributed, raw values were log-transformed. Analysis of covariance (ANCOVA) was used to compare the 6-week values between the groups using the baseline measures as the covariate. Paired samples *t*-test was used for comparing the measurements in the beginning and at the end of the intervention within the study groups. The χ^2 test was used for the comparison of categorical variables. The statistical significance level was set at $p = 0.05$ (two tails).

Results

A total of 100 patients were screened for eligibility and 48 patients entered the study. Six patients were dropped out during the intervention due to low adherence to dietary intervention, travel, and refuse to continue. Therefore, the final study population consisted of 42 subjects; 22 subjects in the OO group, and 20 subjects in the CO group (Figure). Table 1 summarizes the general characteristics of the participants. No significant differences were observed in the baseline characteristics between the two groups.

Baseline levels and 6-week changes in anthropometric measures are shown in Table 2. There were no significant differences between the OO and CO groups concerning the body weight and physical activity at the baseline and after the intervention.

As shown in Table 3, energy and dietary intakes of nutrients did not differ between the groups at the baseline. Dietary intakes of total fat and monounsaturated fat of both groups increased during the intervention due to the consumption of olive and canola oils. However, there were no differences in dietary intakes of the two groups at 6-week.

CO consumption resulted in a significant reduction in plasma Lp-PLA_2 mass ($p = 0.008$) during 6 weeks, whereas the mean changes of IL-6 concentration were significantly lower after OO consumption compared with CO ($p = 0.008$). After 6 weeks of intervention, plasma Lp-PLA_2 activity, C3, C4, and lipid profile had no significant changes in neither groups (Table 4).

Discussion

The present study suggests that a relatively short dietary intervention with refined olive oil can have a significant effect on plasma IL-6 whereas canola oil may impact plasma Lp-PLA_2 mass without changing lipoproteins and other inflammatory biomarkers in patients referred to coronary angiography.

In the present study, the consumption of olive oil had a more lowering effect on plasma IL-6 concentration. The difference in plasma IL-6 levels between the two groups can be related to the difference in fatty acid composition of canola and olive oils. In particular, olive oil consists of 14.5% SFA,

70% oleic acid, 11% linoleic acid, and 1.5% palmitoleic acid, whereas canola oil is characterized by a low level of SFAs (7%); 61% oleic acid, 19% linoleic acid, and 9% alpha-linolenic acid (ALA) [19]. Compared to canola oil, the amount of oleic and palmitoleic acid in olive oil is higher. In vitro studies have shown that the addition of oleic or palmitoleic acid to the cell culture medium is effective in reducing or preventing the increase of IL-6 levels [20-23]. Some human studies have also shown evidence of an inverse association between oleic acid and IL-6 concentration [24].

A growing body of evidence indicates that Lp-PLA_2 represents an independent risk factor for CVD. Lp-PLA_2 belongs to the family of structurally diverse phospholipase A_2 enzymes, also known as platelet-activating factor acetylhydrolase (PAF-AH) [25]. Circulating Lp-PLA_2 is primarily associated with LDL-C, the majority of it is bound to atherogenic small-dense LDL-C particles [26]. The observed decrease in Lp-PLA_2 level following canola oil consumption may be related to its n-3 fatty acid content. Canola oil contains more PUFAs (both n-6 and n-3) and less MUFA than olive oil. In patients admitted to elective coronary angiography, the content of the long-chain n-3 PUFA eicosapentaenoic acid (EPA) in adipose tissue was inversely associated with plasma Lp-PLA_2 mass [27]. Similarly, in participants of the Multi-Ethnic Study of Atherosclerosis, plasma Lp-PLA_2 mass and activity were significantly lower in those with the higher plasma EPA and Docosahexaenoic acid (DHA) [28]. The evidence from intervention trials for the influence of n-3 PUFAs on Lp-PLA_2 is equivocal. In healthy people, two studies have reported no effect of n-3 PUFA supplementation on Lp-PLA_2 [29, 30]. Nelson et al. showed that supplementation with n-3 fatty acids capsules (fish oil or flaxseed oil) over 8 weeks had no significant effect on plasma Lp-PLA_2 mass or activity when compared to control (olive oil capsule supplementation) [29]. In contrast, Asztalos et al. showed that as compared to placebo (6 g/day olive oil) supplementation with the higher dose of EPA (1800 mg), but not DHA or lower dose of EPA (600 mg) over 6 weeks could reduce Lp-PLA_2 mass in a healthy population [31]. Apart from the effects in healthy subjects, an increase in n-3 intake has been shown to decrease Lp-PLA_2 levels in patients with cardiovascular risk factors. In stable CAD patients undergoing percutaneous coronary intervention, administration of omega-3 PUFA (1 g/day) for 4 weeks decreased Lp-PLA_2 mass and activity compared to control (soybean oil capsules) [32]. Similar findings have been observed in patients with diabetes [33] and in subjects who had residual hypertriglyceridemia after receiving statins [34, 35].

The pro-atherogenic role of Lp-PLA_2 could be related to its ability to hydrolysis of oxidized phospholipids on the LDL-C surface, resulting in the generation of two proinflammatory and proapoptotic lipid mediators, lysophosphatidylcholine, and oxidized free fatty acids, which play an important role in the development of atherosclerotic necrotic cores by recruiting and activating macrophages or leukocytes [36]. In the present study, although canola oil reduced the Lp-PLA_2 level, it had no significant effect on inflammatory factors. Consistent with this contention, supplementation with n-3 fatty acids (EPA) has reduced plasma Lp-PLA_2 without significant effects on plasma inflammatory biomarkers, including IL-6 [31].

Complement factors C3 and C4 have been associated with atherosclerosis and cardiovascular risk factors [16] and have shown substantial correlations with cardiovascular risk factors [37]. Plasma C3 and C4 did not change in either group. In a previous study, an increase was observed in the C3 concentrations after the intake of high saturated fat, compared with high-monounsaturated fat [12].

In the current study, neither olive oil nor canola oil consumption had a significant impact on plasma lipids and lipoproteins. Consistent with our findings, in previous studies, the intake of refined OO has not had a significant effect on the plasma TG, LDL-C, or HDL-C levels in mildly hypercholesterolemic subjects who were not on lipid-lowering medications [38] or in stable coronary artery disease patients [39]. However, some previous studies have reported the beneficial effects of CO on plasma lipids [40-43]. Yet, it should be noted that the study population in these studies were healthy people or those with cardiovascular risk factors not on lipid-lowering agents. In contrast, the majority of participants in the present study were under statin therapy and had an optimum level of plasma lipids. Therefore, the beneficial effects of canola oil on plasma lipid profiles appear to be evident in patients whose plasma lipids are high at baseline and are not on lipid-lowering medication. Intake of CO or OO in the context of a lipid-lowering diet for 3.5 weeks in hyperlipidemic subjects who were not on lipid-lowering agents had similar effects on serum lipoprotein concentration [19].

One limitation of this study is the short duration of the dietary intervention. Furthermore, we could not conduct the study in a tightly regulated, controlled feeding design. However, the study oils were provided to individuals (more than each participant's need) and their consumption was monitored weekly. In addition, cross-over study design could have reduced confounding factors associated with the inherited characteristics of the participants. Nevertheless, cross-over studies require that study participants be followed for a longer period and that their treatment plan should not change during this time. Comparison of two commonly consumed edible oils and detailed data collection through face-to-face meetings were important strengths of the current study.

Conclusions

In summary, each of the refined olive or canola oils improved one of the inflammatory CVD risk factors. Regarding the role of the circulating level of IL-6 in the prediction of future coronary heart disease events [44-46], a decrease in IL-6 level following olive oil consumption can reduce the risk of cardiovascular events. On the other hand, canola oil consumption decreased the level of Lp-PLA_2 that its increased levels have been associated with increased risk of cardiovascular events [14]. Overall, consumption of either of the refined olive or canola oils in the context of a healthy diet may have a beneficial effect on the secondary prevention of CVD by improving inflammatory risk factors.

Abbreviations

ALA: alfa-linolenic acid

ANCOVA: analysis of covariance

CABG: coronary artery bypass graft

CAD: coronary artery disease

CO: canola oil

CVD: cardiovascular disease

DHA: docosahexaenoic acid

EPA: eicosapentaenoic acid

HDL-C: high-density lipoprotein cholesterol

IL-6: Interleukin-6

LDL-C: low-density lipoprotein cholesterol

Lp-PLA$_2$: lipoprotein-associated phospholipase A_2

MUFA: monounsaturated fatty acid

OO: olive oil

PUFA: polyunsaturated fatty acid

SFA: saturated fatty acid

TG: triglycerides

Declarations

- **Ethics approval and consent to participate**

The procedures followed in this study were in accordance with the 1964 Helsinki Declaration and the study protocol was approved by the Ethical Committee of National Nutrition & Food Technology Research Institute, Tehran, Iran (the Ethical No: IR.SBMU.NNFTRI.REC.1398.074), and written informed consent were obtained from all patients.

- **Consent for publication**

Not Applicable.

- **Availability of data and materials**

All data generated or analysed during this study are included in this published article [and its supplementary information files].

- **Competing interests**

The authors declare that they have no competing interests.

- **Funding**

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- **Authors' contributions**

NK was responsible for designing the research protocol, writing the protocol, conducting the research, screening potentially eligible studies, conducting biochemical tests, extracting and analyzing data, interpreting results, and writing the paper.

JN was responsible for designing the research protocol and screening of potentially eligible studies. He contributed to extracting and analyzing data, interpreting results, and writing the paper.

AZ assisted in conducting the research, especially in medical consultation & material support, and study supervision.

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Tables

Table 1. Baseline characteristics of the participants [a]

Variable	Olive Oil group (n=22)	Canola Oil group (n=20)	p-value [b]
Age (year)	55.09 ± 6.92	59.30 ± 5.84	0.44
Sex (Male)	20 (91%)	18 (90%)	0.66
PCI history	16 (73%)	16 (80%)	0.89
CABG history	2 (9.1%)	1 (5%)	0.86
Diabetes Mellitus	8 (36%)	8 (40%)	0.91
Hypertension	11 (50%)	11 (55%)	0.92
Dyslipidemia	12 (54%)	8 (40%)	0.55
Overweight	16 (73%)	11 (55%)	0.19
Smoking	8 (36%)	4 (20%)	0.30
Medications:			
Aspirin	21 (95%)	20 (100%)	0.93
Clopidogrel	15 (68%)	10 (50%)	0.29
Statins	20 (91%)	19 (95%)	0.93
ACEI	9 (41%)	4 (20%)	0.12
ARB	10 (45%)	13 (65%)	0.42
BB	15 (68%)	15 (75%)	0.81
Nitrates	7 (31%)	7 (35%)	0.90
Aldosteron Antagonist	5 (22%)	1 (5%)	0.17

[a] Data presented as Mean ± SD or number (percentage).

[b] Data were compared using Independent t-test or Chi-square test.

PCI: Percutaneous Coronary Intervention; CABG: Coronary Artery Bypass Graft; ACEI: Angiotensin Converting Enzyme Inhibitor; ARB: Angiotensin Receptor Blocker; BB: Beta-Blocker.

Table 2. Anthropometric measures and physical activity of the participants [a]

Variable	Time	Olive Oil group (n=22)	Canola Oil group (n=20)	p-value [b]
Body Weight (kg)	Baseline	80.45 ± 11.77	78.65 ± 12.81	0.62
	6-week	80.45 ± 11.49	78.30 ± 12.47	0.64
BMI (kg/m^2)	Baseline	26.91 ± 3.38	27.31 ± 4.39	0.34
	6-week	26.94 ± 3.35	27.19 ± 4.31	0.30
Physical Activity (MET-h/day)	Baseline	27.99 ± 5.23	27.30 ± 3.49	0.65
	6-week	28.01 ± 5.23	27.36 ± 3.57	0.69

[a] All values are Mean ± SD.

[b] Data were compared using Independent t-test.

BMI: Body Mass Index; MET: Metabolic Equivalent.

Table 3. Dietary intake of the participants at the baseline and after the intervention [a]

Variable	Time	Olive Oil group [b] (n=22)	Canola Oil group [b] (n=20)	p-value [c]
Energy (kcal)	Baseline	1781.40 ± 196.10	1767.20 ± 146.19	0.55
	6-week	1850.72 ± 143.20	1801.20 ± 140.44	0.26
Carbohydrate (gr)	Baseline	233.05 ± 32.18	235.20 ± 28.75	0.82
	6-week	234.25 ± 33.57	232.85 ± 29.33	0.73
Carbohydrate (%)	Baseline	51.90 ± 4.60	53.26 ± 5.16	0.38
	6-week	50.47 ± 4.20	51.24 ± 4.97	0.60
Protein (gr)	Baseline	69.75 ± 15.55	74.25 ± 15.12	0.36
	6-week	70.65 ± 11.27	73.30 ± 11.47	0.46
Protein (%)	Baseline	15.51 ± 3.05	16.76 ± 2.84	0.18
	6-week	15.29 ± 2.27	16.26 ± 2.05	0.16
Total Fat (gr)	Baseline	64.30 ± 11.59	59.05 ± 9.93	0.13
	6-week	71.40 ± 7.91 †	68.90 ± 8.36 †	0.33
Total Fat (%)	Baseline	32.17 ± 4.53	30.05 ± 4.15	0.13
	6-week	34.87 ± 4.36 †	34.47 ± 3.83 †	0.75
SFA (gr)	Baseline	16.00 ± 4.56	16.10 ± 5.09	0.94
	6-week	14.90 ± 3.56	13.75 ± 3.37	0.30
SFA (%)	Baseline	7.99 ± 2.01	8.15 ± 2.24	0.82
	6-week	7.28 ± 1.85	6.84 ± 1.44	0.40
MUFA (gr)	Baseline	19.45 ± 6.73	18.45 ± 4.09	0.26
	6-week	30.30 ± 4.37 †	28.50 ± 3.53 †	0.18
MUFA (%)	Baseline	11.18 ± 2.99	10.38 ± 1.90	0.12
	6-week	14.79 ± 2.45 †	14.25 ± 1.59 †	0.10
PUFA (gr)	Baseline	25.10 ± 6.48	22.45 ± 4.11	0.13
	6-week	23.75 ± 4.65	24.40 ± 2.76	0.59
PUFA (%)	Baseline	12.58 ± 3.03	11.47 ± 2.21	0.19
	6-week	11.56 ± 2.16	12.22 ± 1.37	0.25
Cholesterol (mg)	Baseline	167.65 ± 82.15	170.00 ± 55.65	0.91
	6-week	157.00 ± 73.63	167.35 ± 60.39	0.63
Fiber (gr)	Baseline	15.45 ± 2.32	14.60 ± 3.78	0.88
	6-week	15.90 ± 2.78	15.75 ± 3.24	0.87

[a] All values are Mean ± SD.

[b] The daily olive or canola oil consumption is considered.

[c] Data were compared using Independent t-test.

[†] Significantly different from Baseline. Data were compared using Paired t-test.

SFA: Saturated Fatty Acid; MUFA: Monounsaturated Fatty Acids; PUFA: Polyunsaturated Fatty Acids.

Table 4. Measures of biochemical variables by intervention groups [a]

Variable	Olive Oil group (n=22)			Canola Oil group (n=20)			P [c]
	Baseline	6-Week	Δ value [b]	Baseline	6-Week	Δ value [b]	
TC (mg/dL)	116.77 ± 25.15	124.36 ± 28.94	8.45 ± 17.67	136.25 ± 46.45	133.35 ± 47.54	-2.90 ± 16.81	0.10
LDL-C (mg/dL)	63.64 ± 13.72	67.36 ± 17.39	3.68 ± 11.27	74.65 ± 30.46	72.90 ± 28.98	-1.75 ± 9.03	0.16
sd-LDL (mg/dL)	24.14 ± 10.32	23.14 ± 11.18	-0.91 ± 6.34	22.10 ± 7.51	21.00 ± 9.48	-1.10 ± 6.35	0.62
HDL-C (mg/dL)	37.73 ± 7.92	39.50 ± 7.46	1.50 ± 5.80	42.90 ± 6.49	43.15 ± 8.33	0.35 ± 5.21	0.79
TC/HDL-C	3.17 ± 0.47	3.25 ± 0.71	0.08 ± 0.39	3.06 ± 0.72	3.10 ± 0.83	0.03 ± 0.33	0.81
TG (mg/dL)	112.73 ± 33.04	120.50 ± 61.38	7.63 ± 36.45	122.45 ± 31.94	126.05 ± 35.40	3.90 ± 20.92	0.32
Lp-PLA$_2$ mass (ng/mL)	5.66 ± 4.09	6.00 ± 4.51	0.34 ± 1.57	3.96 ± 2.45	2.99 ± 1.65	-0.97 ± 1.84 [†]	0.008
Lp-PLA$_2$ Activity ((nmol/min/mL	0.022 ± 0.013	0.021 ± 0.017	-0.000 ± 0.008	0.012 ± 0.003	0.010 ± 0.004	-0.001 ± 0.002	0.74
(IL-6 (pg/mL	21.95 ± 20.38	12.49 ± 13.70	-9.46 ± 9.46 [†]	19.53 ± 10.52	18.62 ± 8.55	-0.90 ± 6.80	0.008
(C3 (g/L	199.32 ± 35.04	200.68 ± 33.63	1.36 ± 36.64	205.30 ± 44.46	223.50 ± 42.40	18.10 ± 49.00	0.08
(C4 (g/L	38.82 ± 11.99	36.23 ± 9.48	-2.59 ± 9.09	39.20 ± 9.03	34.60 ± 10.35	-4.55 ± 12.43	0.52
C3/C4	5.56 ± 1.98	5.37 ± 2.08	0.23 ± 0.91	5.37 ± 2.08	6.36 ± 2.45	0.99 ± 2.53	0.27

[a] All values are Mean ± SD.

[b] Change of parameter between 6-week and baseline (6-week minus baseline).

[c] The values for 6-week were analyzed using ANCOVA with baseline values as covariate.

† Significantly different from baseline. Data were compared using Paired t-test.

TC: Total Cholesterol; LDL-C: Low Density Lipoprotein-Cholesterol; sd-LDL: Small Dense LDL; HDL: High Density Lipoprotein-Cholesterol; TG: Triglyceride; Lp-PLA_2: Lipoprotein-Associated Phospholipase A_2; IL-6: Interleukin-6.

Figures

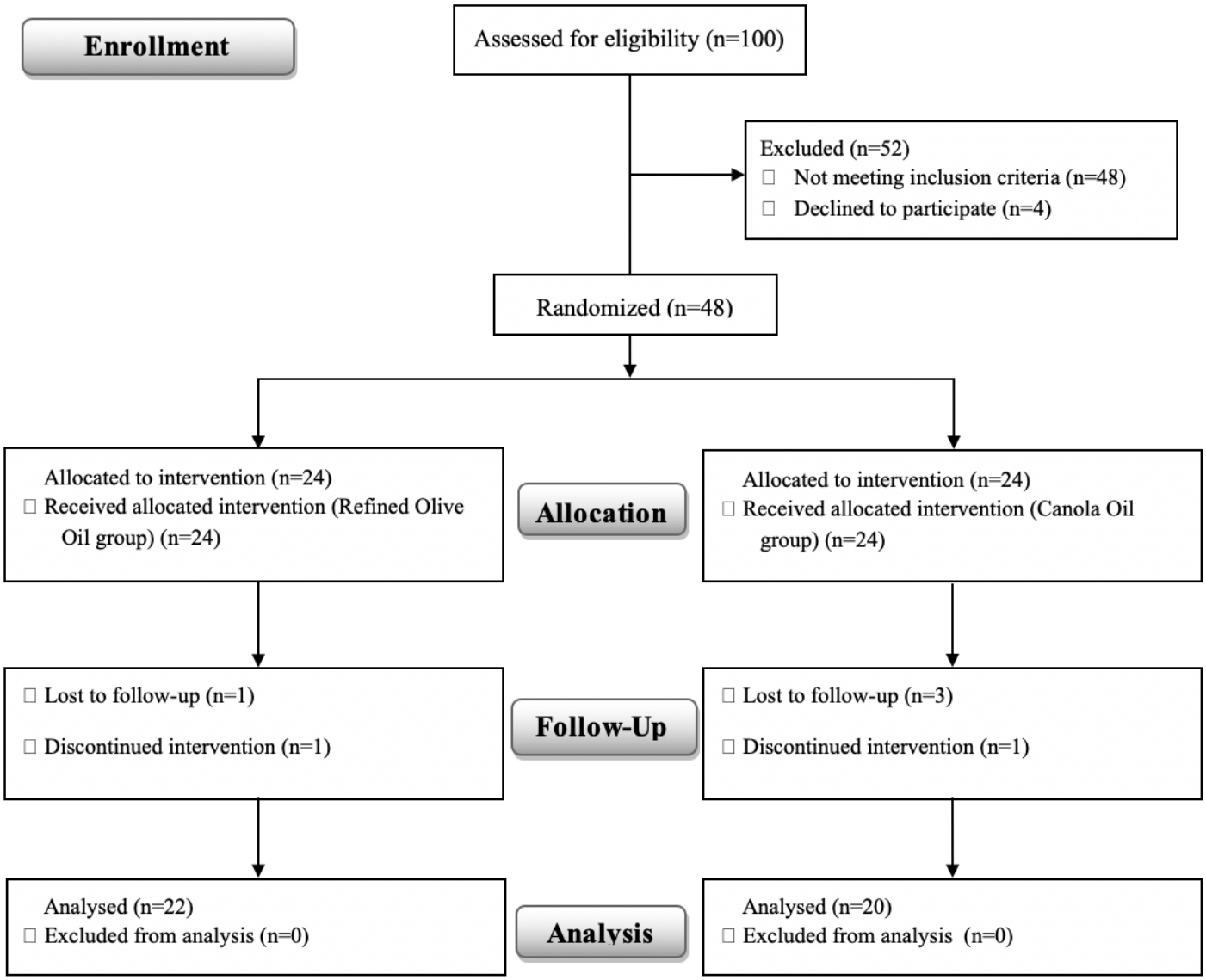

Figure 1

Consort flow diagram of selection and allocation of the participants included in the study

Supplementary Files

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- CONSORT2010Checklist.doc