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Ingestion of moderately thermally oxidized polyunsaturated fat decreases serum resistance to oxidation in men with coronary artery disease[☆]

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Abstract

We have examined the effects of ingesting moderately thermally oxidized and unheated polyunsaturated fatty acid (PUFA)–rich vegetable oils on postprandial oxidative stress, serum and lipoprotein oxidation, paraoxonase-1 activity, and circulating cell adhesion molecules in men with coronary artery disease (CAD) and in healthy controls. Twenty-four men with stable CAD and 20 healthy men were randomized to receive a meal rich in thermally oxidized (1 hour at 180°C) sunflower oil (TSO) or the corresponding unheated oil (USO) in a crossover trial with 1 week between meals. Blood was taken at baseline and 4 and 6 hours after the meals. In men with CAD, the lag time in dilute serum oxidation by copper ions decreased significantly (−16%, $P < .01$) during the TSO meal; and this change was significantly different ($P < .05$) compared with the USO meal. Plasma soluble vascular cell adhesion molecule–1 concentration, a marker of endothelial activation, increased (4%, $P < .05$) significantly during the TSO meal and decreased (−5%, $P < .05$) significantly at 4 hours after the USO meal; and these changes were significantly different ($P = .02$). In both groups of men, plasma peroxides (5%-11%) and vitamin E (6%-12%) increased significantly ($P < .05$) whereas serum paraoxonase-1 activity and oxidized low-density lipoprotein concentration did not change significantly during both meals. This study suggests that ingestion of a PUFA vegetable oil moderately oxidized in line with domestic cooking methods may enhance the postprandial environment for lipoprotein oxidation but not sufficiently to appreciably increase levels of oxidized low-density lipoprotein and endothelial activation in men with CAD. However, it may be prudent for men with CAD to avoid using PUFA-rich vegetable oils in cooking.
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1. Introduction

Vegetable oils rich in polyunsaturated fatty acids (PUFAs) are used in domestic cooking and deep-frying. Polyunsaturated fatty acids are readily oxidized; and when they are heated at frying temperature in air, a variety of lipid oxidation products are formed. Meals rich in oxidized fatty acids increase oxidative stress [1], plasma [2], and lipoprotein [3] content of oxidized fatty acids; intrinsic susceptibility of lipoproteins to oxidation [3]; and endothelial activation [4] and decrease serum paraoxonase-1 (PON-1) arylesterase activity [5] in healthy subjects. In patients with coronary artery disease (CAD), increased systemic oxidative stress [6], high concentrations of vascular cell adhesion molecule–1 (VCAM-1) [7], and low serum PON-1 activity [8] are associated with increased risk of a cardiovascular event. Cell adhesion molecules are markers

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of endothelial activation, and abnormally high levels of the soluble forms of these molecules in the circulation suggest atherosclerotic plaque activation with increased risk of disruption in patients with CAD [9-11]. Oxidized low-density lipoprotein (oxLDL) upregulates expression of cell adhesion molecules on endothelial cells [12], and high plasma and plaque levels are associated with increased vulnerability of atherosclerotic lesions [13]. Paraoxonase-1 is a circulating antioxidant enzyme that is capable of hydrolyzing specific oxidized lipids in lipoproteins [14] and protects LDL from oxidation [15]. Lipoprotein oxidation in vivo is influenced by a number of anti- and pro-oxidant factors, some of which may affect serum resistance to copper ion oxidation in vitro. Meals rich in oxidized fatty acids can modify factors that have the potential to impact on arterial metabolism and function and atherosclerotic lesion stability in patients with CAD.

Delayed clearance of triacylglycerol (TAG)-rich lipoproteins in the postprandial period after a fatty meal is thought to increase vascular injury and atherosclerosis [1,16]. Impaired clearance of postprandial TAG-rich lipoproteins may increase the opportunity for absorbed oxidized lipids to promote lipoprotein oxidation and vascular injury. In patients with CAD, clearance of remnant lipoproteins derived from lipolysis of postprandial TAG-rich lipoproteins is delayed [17]. These patients are advised to replace saturated fats with PUFAs and monounsaturated fats in the diet, and this includes use in cooking. However, there is little information available on the effects of meals rich in oxidized PUFAs on postprandial oxidative stress and factors linked to lipoprotein oxidation, antioxidant protection, and endothelial activation in patients with CAD. The purpose of the present study was therefore to determine the effects of a PUFA vegetable oil that had been moderately thermally oxidized in keeping with domestic cooking methods and the corresponding unheated oil on serum resistance to oxidation and PON-1 arylesterase activity and on plasma concentrations of peroxides, antioxidants, oxidized LDL (oxLDL-4E6), and soluble cell adhesion molecules during the postprandial period in men with CAD and in healthy controls.

2. Subjects and methods

2.1. Subjects

Twenty-four men aged 49 to 68 years with stable angina and angiographically proven *CAD* defined as one or more stenoses >50% arterial diameter were recruited from the Cardiovascular Clinic of the Cardiology Department, Dunedin Hospital. Exclusion criteria included myocardial infarction within the preceding 3 months; presence of unstable angina, coronary artery bypass grafting, heart failure, or other serious illnesses; smoking cigarettes; and use of antioxidant supplements. Twenty men aged 47 to 75 years and without a history of serious illness were recruited from advertisements and from the staff of the University of Otago. None smoked cigarettes, and none was taking antioxidant supplements. All participants gave written and informed consent before commencing the study that was approved by the Otago Ethics Committee.

2.2. Study design

The study had a single-blind, randomized, crossover design. Participants were randomized to receive a meal rich in thermally oxidized sunflower oil (TSO) or a similar meal containing unheated sunflower oil (USO) in place of the heat-modified oil. At least 1 week later, they consumed the alternate meal. The men with CAD were studied first. After an overnight fast, participants reported to the study center in the early morning (8:00 AM). The CAD patients were instructed to delay taking their medications until after the 6-hour study period. Meals were consumed within 15 minutes. Participants were instructed not to consume other foods or beverages other than water and not to perform strenuous physical exercise during the study period. Blood was taken immediately before and at 4 and 6 hours after the participants had consumed the meals.

2.3. Meals

Sunflower oil was heated in a small electrical household deep-fryer for 1 hour at 180°C. The heated oil was stored at 4°C in the dark until it was used in the preparation of the meals. Several batches of TSO were prepared during the study. The contents of lipid oxidation products and vitamin E in TSO and USO are shown in Table 1. The content of lipid oxidation products was higher and the content of vitamin E was lower in TSO compared with USO. The meals consisted of 200 g reconstituted instant mash potato (40 g "Cinderella" dehydrated potato plus 160 mL water) plus TSO or USO at 0.6 g/kg body weight. The composition of the meals calculated on the basis of 60-g test fat was as follows: carbohydrate, 20% energy; protein, 2% energy; fat, 78% energy; and total energy, 2876 kJ.

2.4. Laboratory methods

2.4.1. Blood collection

Venous blood was taken into tubes containing solid dipotassium EDTA or into plain tubes. Plasma and serum were prepared by centrifuging the tubes at 1500*g* for 15 minutes at 4°C. Aliquots of plasma and serum were immediately stored at −80°C.

Table 1
Lipid oxidation products and vitamin E in the test fats

	TSO	USO
	Mean ± SD (n = 5)	
Conjugated dienes (μmol/kg)	29.8 ± 5	19.7
Peroxides (mmol/kg)	8.5 ± 1.4	7.2
Carbonyls (mmol/kg)	6.7 ± 1.1	3.9
Vitamin E (mmol/kg)	0.87 ± 0.17	1.14

2.4.2. Plasma lipids, lipoproteins, and apolipoprotein B

High-density lipoprotein cholesterol (HDL-C) was measured in the supernatant after precipitation of apolipoprotein B (apoB)–containing lipoproteins in plasma [18]. Cholesterol and TAG were measured in plasma and plasma fractions using commercial enzymatic kits (Roche/Boehringer, Mannheim, Germany) and automated methods. Plasma apoB concentration was also measured by automated methods using a commercial kit (Roche/Boehringer).

2.4.3. Peroxides, antioxidants, serum oxidation, oxLDL-4E6, and PON-1

Plasma peroxides were measured by an enzymatic method using horseradish peroxidase as described previously [19] with an incubation time of 45 minutes. The coefficient of variation for this measurement was 3%. Plasma vitamin E concentration was measured colorimetrically as described previously [20]. Plasma uric acid was measured by an automated method using the Hitachi E170 platform (Roche Diagnostics, Basel, Switzerland) in the laboratories of Otago Diagnostic Service. Oxidation of dilute serum with copper ions was performed as described previously [21] on serum that had been stored overnight at −80°C. The lag time in conjugated diene formation was calculated and was used as a measure of susceptibility of serum to oxidation. Plasma oxLDL-4E6 concentration was measured in duplicate by immunoassay using the mB-4E6 monoclonal antibody to copper ion oxidized LDL in a commercial kit (Mercodia, Uppsala, Sweden). Intra-assay coefficient of variation for this assay is 6%. Serum PON-1 arylesterase was measured as described previously [5]. The method has an intra-assay coefficient of variation of 5%.

2.4.4. Cell adhesion molecules

Plasma VCAM-1 and intercellular adhesion molecule-1 (ICAM-1) concentrations were measured in duplicate by immunoassay using commercial kits (R&D Systems, Minneapolis, Minn). Intra-assay coefficients of variation for these assays are 5%. All samples from an individual were measured in the same analytical run for the assay of cell adhesion molecules, oxLDL-4E6, and several other variables.

2.4.5. Lipid oxidation products and vitamin E in test fats

Lipid oxidation products including conjugated dienes, peroxides, and carbonyls were measured in TSO and USO. Conjugated dienes were measured at 234 nm in a hexane solution of the oils, and the molar absorption coefficient for conjugated dienes (29 500 L mol^{-1} cm^{-1}) was used to calculate diene content in micromoles per kilogram. Peroxides in the oils were measured using the American Oil Chemists Association standard iodide method (official method Cd-8-53 for peroxide value). The carbonyl content of the oils was determined by a quinoidal ion method using 2,4-dinitrophenylhydrazine in propan-2-ol [22]. Vitamin E content of the test fats was measured by reverse-phase high-performance liquid chromatography as described previously [23].

2.5. Statistical analysis

The SPSS 11 statistical package (SPSS, Chicago, Ill) was used to analyze the data. Skewed data were log-transformed before statistical analysis. Values are mean ± SD unless stated otherwise. Repeated-measures analysis of variance (ANOVA) was used to test data for effects of the type of meal, the time after ingestion of the meals, and the interaction between these factors. The model included the type of meal and time after the meals as within-subject factors and order of the meals as a between-subjects factor. Within-subjects time contrast in repeated-measures ANOVA was used to detect variations in the data with time. Paired *t* tests were used for comparisons between baseline and postprandial values only when a significant meal × time interaction was detected in the data. Data from men with CAD and healthy men were analyzed separately. Student *t* test was used to compare mean values from unpaired data. Spearman rank correlation coefficients were used to test for associations between variables. Two-sided tests of significance were used, and a P value of $<.05$ was considered to be statistically significant.

3. Results

3.1. Baseline characteristics

The baseline characteristics of the participants are summarized in Table 2. On average, the CAD patients were 4 years older than the healthy subjects. All but one healthy subject (aged 47 years) was in the same age range as the CAD patients. Plasma total cholesterol (TC), apoB, and HDL-C were lower in men with CAD. All but one of the CAD patients were receiving treatment with a statin drug. The pattern of drug therapy was in keeping with current clinical practice.

Table 2
Baseline characteristics of the men with CAD and the healthy men

	Men with CAD (n = 24)	Healthy men (n = 20)
Age (y)	60 ± 6	56 ± 7
Body weight (kg)	83.8 ± 13.1	86.2 ± 15.7
BMI (kg/m^2)	27.7 ± 4.0	27.3 ± 3.9
TC (mmol/L)	4.26 ± 0.70	5.83 ± 0.93
TAG (mmol/L)	1.64 ± 1.01	1.41 ± 0.60
HDL-C (mmol/L)	1.11 ± 0.22	1.34 ± 0.30
MI (%)	54	
Aspirin (%)	100	
Statins (%)	96	
ACE inhibitors (%)	29	
Oral nitrates (%)	33	
β-Blockers (%)	71	

Values are mean ± SD.
BMI indicates body mass index; MI, myocardial infarction; ACE, angiotensin-converting enzyme.

Table 3
Plasma lipids, HDL-C, and apoB during the meals

	Time (h)	Men with CAD (n = 24)			Healthy men (n = 20)		
		TSO	USO	P*	TSO	USO	P
TAG (mmol/L)	0	1.65 ± 0.90	1.64 ± 0.75		1.46 ± 0.57	1.38 ± 0.64	
	4	1.85 ± 0.98†	1.95 ± 1.04†	.87	1.73 ± 0.78†	1.57 ± 0.69†	.85
	6	1.83 ± 1.20	1.76 ± 0.97		1.58 ± 0.71	1.47 ± 0.71	
TC (mmol/L)	0	4.37 ± 0.69	4.21 ± 0.71		5.79 ± 0.92	5.81 ± 0.90	
	4	4.38 ± 0.63	4.34 ± 0.75†	.13	5.93 ± 0.99	5.88 ± 0.94	.67
	6	4.40 ± 0.70	4.30 ± 0.72		5.86 ± 0.96	5.87 ± 0.91	
HDL-C (mmol/L)	0	1.12 ± 0.22	1.10 ± 0.23		1.34 ± 0.26	1.34 ± 0.29	
	4	1.15 ± 0.23†	1.14 ± 0.23†	.55	1.36 ± 0.30	1.37 ± 0.30	.93
	6	1.16 ± 0.20†	1.13 ± 0.24†		1.37 ± 0.31†	1.39 ± 0.32†	
Apo B (g/L)	0	0.94 ± 0.21	0.87 ± 0.20		1.26 ± 0.29	1.19 ± 0.31	
	4	0.91 ± 0.26	0.86 ± 0.19	.30	1.19 ± 0.30	1.22 ± 0.27	.35
	6	0.88 ± 0.25	0.88 ± 0.23		1.22 ± 0.29	1.25 ± 0.27	

Values are mean ± SD.
* Significance of meal × time interactions in repeated-measures ANOVA.
† $P < .01$ compared with baseline in combined data from both meals using within-subject contrasts in repeated-measures ANOVA.

3.2. Plasma lipids and lipoproteins

Table 3 shows the concentrations of plasma lipids, lipoproteins, and apoB during the study. In men with CAD and healthy men, plasma TAG concentration and plasma HDL-C increased significantly during 4 hours after both meals; and this response was not significantly different between the meals.

3.3. Markers of oxidative stress, oxLDL-4E6, and PON-1 activity

Table 4 shows plasma concentrations of markers of oxidative stress and oxLDL-4E6 and serum PON-1 activity during the meals. In men with CAD and in healthy men, plasma peroxides concentrations increased significantly and plasma uric acid concentration decreased significantly during 4 hours after both meals; and plasma vitamin E concentration increased significantly at 4 and 6 hours after both meals. Serum PON-1 activity and the plasma oxLDL-4E6/apoB ratio did not change significantly during the meals. At baseline, plasma oxLDL-4E6 concentration was significantly lower (40.2 ± 15.3 U/L vs 57.8 ± 19.0 U/L, $P = .001$) in men with CAD compared with healthy men.

3.4. Serum resistance to oxidation

The effect of the meals rich in TSO and USO on the resistance of dilute serum to copper ion oxidation is shown in Fig. 1. In men with CAD, the lag time in dilute serum oxidation decreased significantly (time contrasts with baseline $P = .004$) during the TSO meal and did not change significantly during the meal rich in unheated fat; and these changes were significantly ($P = .049$) different between the meals. In healthy men, the lag time in dilute serum oxidation did not change significantly during the

Table 4
Plasma markers of oxidative stress, serum PON-1 arylesterase activity, and oxLDL concentration during the meals

	Time (h)	Men with CAD (n = 24)			Healthy men (n = 20)		
		TSO	USO	P*	TSO	USO	P
Peroxides (μmol/L)	0	154 ± 74	147 ± 61		181 ± 80	175 ± 67	
	4	167 ± 81†	154 ± 63†	.42	201 ± 93‡	195 ± 73‡	.99
	6	158 ± 81	145 ± 64		186 ± 77†	187 ± 69†	
Uric acid (μmol/L)	0	358 ± 67	356 ± 53		361 ± 66	357 ± 69	
	4	352 ± 63‡	352 ± 55‡	.22	351 ± 65†	348 ± 66†	.91
	6	355 ± 60	356 ± 55		355 ± 64	354 ± 69	
Vitamin E (μmol/L)	0	47 ± 15	45 ± 12		50 ± 11	51 ± 12	
	4	50 ± 17‡	48 ± 15‡	.96	51 ± 10‡	54 ± 12‡	.60
	6	52 ± 17‡	49 ± 10‡		53 ± 10‡	57 ± 13‡	
PON-1 (μmol/[mL min])	0	83 ± 18	84 ± 21		97 ± 29	87 ± 23	
	4	83 ± 18	84 ± 20	.79	93 ± 31	88 ± 21	.47
	6	82 ± 19	81 ± 19		87 ± 30	87 ± 22	
OxLDL-4E6/apoB (U/g)	0	45 ± 16	50 ± 20		46 ± 12	49 ± 14	
	4	48 ± 17	47 ± 16	.10	46 ± 11	46 ± 11	.40
	6	48 ± 22	48 ± 23		47 ± 12	45 ± 10	

Values are mean ± SD.
* Significance of meal × time interactions in repeated-measures ANOVA.
† $P < .05$ compared with baseline in combined data from both meals using within-subject contrasts in repeated-measures ANOVA.
‡ $P < .01$ compared with baseline in combined data from both meals using within-subject contrasts in repeated-measures ANOVA.

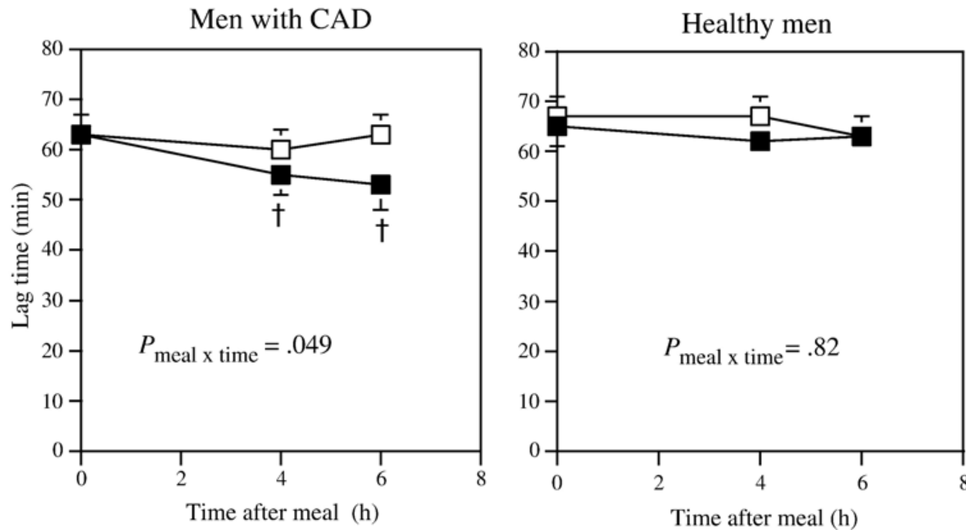

Fig. 1. Lag time in dilute serum oxidation with copper ions in men with CAD and in healthy men after ingestion of meals rich in TSO (■) and USO (□). Values are mean ± SEM. †$P < .01$ compared with baseline using paired t test.

meals. At baseline (the first visit to the study center), the lag times were not significantly ($P = .89$) different in men with CAD (64 ± 19 minutes) compared with healthy men (65 ± 15 minutes).

3.5. Cell adhesion molecules

Table 5 shows the effect of the meals on plasma concentrations of soluble cell adhesion molecules. In men with CAD, plasma VCAM-1 concentration increased significantly ($P = .02$) during 4 hours after the TSO meal and decreased significantly during 4 ($P = .03$) and 6 hours ($P = .04$) after the USO meal; and these changes with time were significantly different between the meals ($P = .02$). There was a significant meal × time interaction without significant changes from baseline during the meals in the VCAM-1 data for healthy men. Furthermore, there was a significant ($P = .01$) time × order of meals interaction for VCAM-1 concentrations and a significant ($P = .049$) meal × time × order interaction for ICAM-1 concentrations in the healthy men.

There were no significant interactions with order of meals in the response of all study variables in men with CAD and all but VCAM-1 and ICAM-1 in healthy men. This implies that washout was adequate for most variables because these interactions incorporate carryover effects.

3.6. Correlations

The 6-hour increase in the lag time in dilute serum oxidation was correlated significantly ($r = 0.655$, $P = .001$) with the corresponding change in serum PON-1 activity during the TSO meal in men with CAD (Fig. 2). The mean decrease in lag time was significantly ($P = .03$) larger in those who showed a decrease (−18 ± 16 minutes, n = 9) compared with those who showed no change or an increase (−4 ± 7 minutes, n = 15) in serum PON-1 during the meal. These 6-hour changes in lag time and PON-1 activity during the TSO meal were not significantly different in those who had a previous myocardial infarction or received therapy with angiotensin-converting enzyme inhibitor drugs, oral nitrates, or β-blocking drugs (data not shown).

At baseline, the lag time in dilute serum oxidation was correlated significantly with plasma peroxide concentration (men with CAD: $r = -0.715$, $P < .001$; healthy men: $r = -0.521$, $P = .02$; all men: $r = -0.595$, $P < .001$) and plasma uric acid concentration (men with CAD: $r = 0.583$, $P = .003$; all men: $r = 0.504$, $P < .001$). The

Table 5
Plasma concentrations of soluble cell adhesion molecules during the meals

	Time (h)	Men with CAD (n = 24)			Healthy men (n = 20)		
		TSO	USO	P*	TSO	USO	P*
VCAM-1 (μg/L)	0	553 ± 77	582 ± 106		612 ± 147	565 ± 123	
	4	573 ± 81†	555 ± 92†	.02	583 ± 107	575 ± 125	.04
	6	558 ± 103	559 ± 87†		587 ± 127	559 ± 113	
ICAM-1 (μg/L)	0	273 ± 50	270 ± 46		257 ± 38	247 ± 30	
	4	279 ± 51	275 ± 48	.52	257 ± 37	252 ± 32	.79
	6	280 ± 58	273 ± 51		251 ± 31	246 ± 29	

Values are mean ± SD.
* Significance of meal × time interaction in repeated-measures ANOVA.
† $P < .05$ compared with baseline (paired t test).

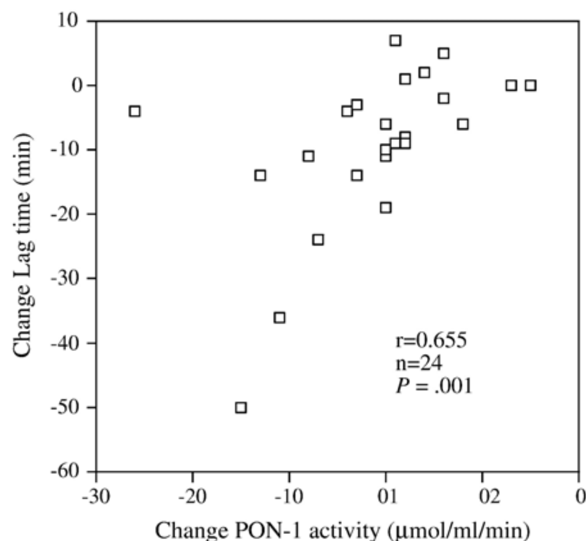

Fig. 2. Correlation between 6-hour changes in lag time in dilute serum oxidation and PON-1 arylesterase activity after the meal rich in TSO in men with CAD.

correlation between the lag time and plasma uric acid in healthy men did not attain statistical significance (r = 0.350, P = .13). Plasma vitamin E concentration was not correlated significantly with lag time at baseline (all men: r = 0.151).

4. Discussion

Our data indicate that resistance of postprandial serum to copper ion oxidation decreased during 6 hours after a meal rich in a thermally oxidized PUFA-rich vegetable oil in men with CAD. This decrease in serum resistance to oxidation was associated with change in serum PON-1 activity and was independent of the increase in plasma peroxides and vitamin E and the decrease in plasma uric acid levels that occurred similarly in both men with CAD and healthy men during meals rich in thermally oxidized and unoxidized PUFA vegetable oils.

An earlier study from our laboratory reported a decrease in serum resistance to oxidation in healthy men during liquid meals rich in thermally oxidized and unheated PUFA vegetable oil [21]. However, the meals in the present study contained solid foods, had lower levels of lipid oxidation products, and induced an approximately 2-fold smaller increase in postprandial lipemia. The postprandial decrease in serum resistance to oxidation after a meal rich in a thermally oxidized PUFA vegetable oil in men with CAD but not in healthy men in the present study suggests that men with CAD may be more susceptible to thermally oxidized PUFAs in the context of domestic cooking.

The presence of CAD and/or associated factors may contribute to the decrease in serum resistance to oxidation in men with CAD during the TSO meal. Atherosclerotic endothelium generates abnormally high levels of oxidants [24] that may conceivably interact with lipid oxidation products absorbed from meals rich in thermally oxidized PUFAs and increase serum susceptibility to oxidation. Furthermore, clearance of postprandial TAG-rich lipoprotein remnant particles is abnormally delayed in patients with CAD [17]; and these particles have pro-oxidant characteristics [25] that may be enhanced by ingested oxidized PUFAs. In the present study, the men with CAD were receiving several medications, some of which are known to influence lipid oxidation [26-28]. Thus, we cannot entirely exclude the possibility of an interaction between medications and ingested oxidized fat leading to decreased serum resistance to oxidation. However, these medications did not directly or acutely affect postprandial serum resistance to oxidation. Serum resistance to oxidation did not vary appreciably during the meal rich in USO, and the study was designed to minimize the acute effect of medications during the meals. Furthermore, the drug regimen did not change during the study.

A decrease in serum resistance to oxidation can occur as a result of an increase in the intrinsic susceptibility of serum lipoproteins to oxidation and/or a decrease in water-soluble antioxidant protection. In the present study, the decrease in serum resistance to oxidation during the TSO meal in men with CAD seemed to be at least partly due to an increase in intrinsic susceptibility of serum lipoproteins to oxidation. Altered intrinsic susceptibility to oxidation probably mediated the association between this decrease in serum resistance to oxidation and change in serum PON-1 activity in our data. The PON-1 enzyme hydrolyses specific oxidized lipids in lipoproteins [14] and protects serum lipoproteins from oxidation [15,29]. The amount of lipid peroxidation in human serum induced by 2,2 azobis-2-amidinopropane hydrochloride in vitro is inversely correlated with serum PON-1 activity [29]. In the present study, the larger decrease in serum susceptibility to oxidation in men with CAD who showed a decrease in serum PON-1 during the TSO meal is consistent with the protective effect of PON-1 against serum lipoprotein oxidation. However, mean serum PON-1 activity did not change appreciably during the meals. Thus, the change in serum PON-1 activity was not primarily responsible for the decrease in serum resistance to oxidation during the TSO meal. Although plasma peroxides and uric acid concentrations were determinants of fasted serum resistance to oxidation, the small postprandial increase in plasma peroxides and decrease in uric acid did not seem to decrease serum resistance to oxidation during the meals. Plasma peroxides increased and uric acid decreased during both TSO and USO meals in men with CAD and healthy men, but serum resistance to oxidation only decreased during the TSO meal in men with CAD. These data suggest that a decrease in water-soluble antioxidants may not have been a predominant cause of the decrease in serum resistance to oxidation. Uric acid is a water-soluble antioxidant and the major determinant of fasted serum resistance to oxidation in nonsmoking individuals [30]. Vitamin E concentration

seems to have less influence on serum resistance to oxidation [30] and was unrelated to baseline resistance of fasted serum to oxidation in our data. The factors responsible for the postprandial decrease in serum resistance to oxidation in men with CAD during a meal enriched in thermally oxidized PUFAs remain to be identified.

Meals rich in fat and fatty, fried, and fast foods poor in antioxidants increase postprandial oxidative stress as indicated by plasma lipid peroxides and urinary 8-isoprostanes [2,31,32]. In the present study, there were proportionally smaller increases in postprandial oxidative stress as indicated by small increases in plasma peroxides and decreases in uric acid concentrations during TSO and USO meals. These increases in oxidative stress were not clearly different between the meals, suggesting that moderate thermal oxidation in line with domestic cooking methods did not appreciably enhance the effect of ingested PUFA vegetable oil on postprandial oxidative stress. It is possible that insufficient thermal oxidation of the vegetable oil and/or the postprandial increase in plasma vitamin E concentration may have attenuated the increase in oxidative stress after ingestion of the TSO and USO meals. The increase in plasma vitamin E is presumably due to the vitamin E content of the test fats. Sunflower oil is rich in vitamin E, and our data and previous research [33] show that substantial quantities remain in sunflower oil that has been heated at frying temperature for 1 hour.

In men with CAD, plasma VCAM-1 concentration responded differently to the meals, with an increase 4 hours after the TSO meal and a decrease from baseline after the USO meal. However, these changes in VCAM-1 were small; and differences in baseline concentrations between the meals complicate their interpretation. Statin therapy may have attenuated postprandial changes in cell adhesion molecules in the men with CAD. A previous study has reported that statin therapy reduces postprandial increases in cell adhesion molecules induced by fatty meals [34]. The effect of fatty meals on plasma VCAM-1 levels in healthy subjects is controversial. In the present study, plasma soluble cell adhesion molecule concentrations did not vary appreciably during meals rich in TSO and USO. Consistent with this finding, plasma VCAM-1 levels did not vary appreciably in healthy subjects during 6 hours after a meal rich in fat from fast foods in a previous study [32]. In contrast, plasma VCAM-1 increased during 4 hours after a meal rich in fat mainly from sausages [4]. Differences in the type of fat and other components of the meals may contribute to this variation in postprandial response of cell adhesion molecules to fatty meals among studies in healthy subjects.

This study has limitations. The number of subjects was relatively small. Thus, care must be taken in extrapolating the findings to larger populations of men. The lower basal concentrations of plasma TC, oxLDL-4E6, and peroxides in the men with CAD compared with the healthy men are probably due to statin therapy. Treatment with statin drugs not only decreases plasma lipids but also decreases plasma concentrations of oxLDL-4E6 [35]. The antioxidant effect of statins [26] may tend to decrease plasma peroxides. However, statins and the other drugs taken by the men with CAD in the present study are now a standard part of the clinical management of patients with CAD.

In conclusion, our data indicate that in men with CAD but not in healthy men, ingestion of a PUFA-rich vegetable oil that has been subjected to moderate thermal oxidation in keeping with many domestic cooking practices increases the susceptibility of serum lipoproteins to copper ion oxidation and especially in those who show a concomitant decrease in activity of the antioxidant PON-1 enzyme. This decrease in serum resistance to oxidation may indicate an in vivo environment conducive of lipoprotein oxidation but not sufficient to acutely increase circulating levels of oxidized LDL. A previous study has reported lower resistance of serum to copper ion oxidation associated with higher mortality from coronary heart disease in Lithuanian compared with Swedish middle-aged men [36]. Whether a postprandial decrease in serum resistance to copper ion oxidation after ingestion of a thermally oxidized PUFA vegetable oil influences cardiovascular risk in men with CAD remains to be determined. Our data suggest that it may be prudent for patients with CAD receiving standard medications to avoid using PUFA-rich vegetable oils in cooking.

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