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Flow-Mediated Dilatation Is Impaired by a High-Saturated Fat Diet but Not by a High-Carbohydrate Diet

Jennifer B. Keogh, Jessica A. Grieger, Manny Noakes, Peter M. Clifton

Objective—It is unknown whether a low-fat diet, which may elevate triglycerides and lower high-density lipoprotein (HDL) cholesterol, harms the endothelium. Our aim was to determine whether a low-fat, high-carbohydrate (CARB) diet impaired endothelial vasodilation compared with high saturated fat (SFA), monounsaturated fat (MUFA), or polyunsaturated fat (PUFA) diets.

Methods and Results—Forty healthy subjects were randomly crossed over to 4, 3-week isocaloric diets high in PUFA, MUFA, or SFA, containing at least 25 g of the relevant fat or a low-fat, CARB, high-glycemic load diet. Flow-mediated dilatation (FMD), fasting blood lipids, high sensitivity C-reactive protein, plasma intercellular, and vascular adhesion molecules plasma E- and P-selectin were measured after each intervention. SFA impaired FMD compared with all other diets ($5.41 \pm 2.45\%$ versus $10.80 \pm 3.69\%$; $P=0.01$). FMD did not change on CARB relative to MUFA or PUFA, despite 23% to 39% rises in triglyceride and 10% to 15% falls in HDL cholesterol. P-selectin was highest after SFA (121 ± 52.7 ng/mL) versus MUFA (98 ± 44.5 ng/mL; $P=0.001$) and PUFA (96 ± 36.4 ng/mL; $P=0.001$).

Conclusion—High SFA caused deterioration in FMD compared with high PUFA, MUFA, or CARB diets. Inflammatory responses may also be increased on this diet. (*Arterioscler Thromb Vasc Biol.* 2005;25:1274-1279.)

Key Words: endothelium ■ diet ■ saturated fat ■ P-selectin ■ FMD

Atherosclerosis is a complex mix of lipid accumulation, inflammation, and cellular proliferation.¹ Endothelial dysfunction precedes the appearance of clinical cardiovascular disease and may be involved in its pathogenesis.² NO, a potent vasodilator and inhibitor of platelet adhesion and aggregation, has an important role in protecting the endothelium.³ Risk factors for coronary atherosclerosis, such as hypercholesterolemia, impair NO bioactivity, leading to endothelial dysfunction⁴ characterized by impaired vasodilation, increased adhesion molecule expression, and enhanced risk of thrombosis.⁵

Cross-sectional studies have shown that endothelial function measured by flow-mediated dilatation (FMD) is impaired in patients with low high-density lipoprotein (HDL) cholesterol,⁶⁻⁸ and improvement in endothelial function has been shown when HDL cholesterol (HDL-C) levels increased after treatment with niacin.⁹ These data suggest that when HDL-C falls, the endothelium may be adversely affected. It has also been reported that endothelium-dependent vasorelaxation is impaired in subjects with hypertriglyceridemia.¹⁰

The effect on FMD of medium-term dietary change has not been extensively examined, and the evidence is conflicting.¹¹⁻¹⁴ Fuentes et al found that FMD improved on a Mediterranean diet but not on a low-fat diet compared with a high saturated fat (SFA) diet,¹¹ whereas de Roos et al

observed no difference in FMD after either a low-fat diet, which increased triglycerides (TG) and lowered HDL-C, or a high monounsaturated fat (MUFA) diet.¹² Ros et al observed improvements in FMD on a high polyunsaturated fat (PUFA) diet compared with a Mediterranean diet.¹³ In a study comparing the effect on FMD of a high trans fatty acid diet with a high SFA diet, de Roos et al observed that FMD was impaired by the high trans fatty acid diet which, also caused a fall in HDL-C.¹⁴ Thus, it is unclear whether all low-density lipoprotein (LDL) cholesterol-lowering diets such as high-carbohydrate (CARB) diets, which also reduce HDL-C and increase TG, or diets high in unsaturated fat, which elevate HDL-C and lower TG, have equivalent effects on endothelial function.

The aim of this study was to determine whether a low-fat CARB diet impaired endothelial vasodilation compared with diets high in SFA, MUFA, or PUFA. Our primary hypothesis was that reductions in HDL-C and increases in LDL cholesterol (LDL-C) induced by dietary manipulation would have an adverse effect on FMD. In addition, given the reported relationship between adhesion molecules and inflammatory markers and acute cardiovascular events,^{15,16} we hypothesized that FMD would be negatively related to adhesion molecules, high sensitivity C-reactive protein (CRP), and pulse wave velocity (PWV), a measure of arterial stiffness.

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TABLE 1. Test Foods for Each Dietary Intervention

Diet	Test Foods (daily)	Energy, kJ	FAT, g	PUFA, g	MUFA, g	SFA, g	CARB, g
PUFA	Polyunsaturated margarine 20 g walnuts 35.00	1595.50	40.32	24.55	9.22	4.68	1.15
MUFA	Canola margarine 20 g almonds 45 g	1695.90	40.90	9.35	26.33	4.14	2.16
CARB	Jam/marmalade 60 g Sultanas 70 g	1550.00	0.28	*	*	*	92.88
SFA	Regular butter 50 g	1525.00	41.00	1.05	10.85	27.00	*

*Negligible fatty acid or carbohydrate composition.

Methods

Subjects

A total of 74 adults answered a newspaper advertisement seeking healthy adults aged 20 to 75 years, and 59 returned a health questionnaire. Inclusion criteria were that volunteers with no history of metabolic disease understand the procedures involved and agree to participate in the study by giving full informed, written consent. Exclusion criteria were type 1 and 2 diabetes (excluded on history and fasting blood sugar at baseline), liver, renal or unstable heart disease, use of long-acting nitrates, sildenafil, or tadalafil, a previous adverse reaction to glyceryl trinitrate (GTN), unstable blood pressure, frequent syncope, and inability to manage study requirements. Volunteers who drank >10 standard drinks per week and whose exercise patterns varied widely were also excluded. Volunteers on lipid-lowering and antihypertensive agents and antioxidant vitamins were included in the study provided that the dose remained stable over the 12-week period and the systolic blood pressure was ≤ 130 mm Hg. Nine volunteers did not meet the selection criteria. Fifty volunteers were admitted to the study; 8 withdrew before study commencement because of travel and health reasons, and 2 withdrew before study completion because of personal problems unrelated to the dietary interventions. Forty subjects (19 men and 21 women) completed the study. At baseline, subjects were 55.9 ± 10.7 years and 79.83 ± 17.35 kg, with a body mass index of 27.26 ± 5.10 kg/m², HDL-C was 1.47 ± 0.42 mmol/L, TG 1.68 ± 1.44 mmol/L, LDL-C 3.29 ± 0.93 mmol/L, and total cholesterol (TC) 5.52 ± 0.87 mmol/L.

Two male volunteers were taking lipid-lowering agents, and 1 male was taking antihypertensive medication; 2 males and 1 female were smokers, 3 females were taking hormone replacement therapy, and 17 subjects, 14 of whom were women, were taking vitamin, mineral, or fish oil supplements. Volunteers were asked to maintain medication and supplements unchanged throughout the study. All studies were done in the fasting state before taking any medication.

Volunteers were asked to keep alcohol intake and physical activity constant during the study.

The protocol was approved by the Commonwealth Scientific and Industrial Research Organization (CSIRO), Health Sciences, and Nutrition Human Ethics Committee. All subjects provided written informed consent.

Study Methodology

This was a randomized, crossover design study of 4, 3-week dietary interventions, with no wash-out periods between interventions. Subjects returned at the end of each intervention for a fasting venous blood sample and weight, FMD, and PWV measurements.

Diets

The dietary interventions were high PUFA, high MUFA, high SFA, and CARB low-fat high-glycemic load diet. In an outpatient setting, subjects were given test foods at 2 weekly intervals to consume daily to achieve the desired fatty acid and carbohydrate content of the diet while also consuming an ad libitum low-fat diet. Test foods were 20 g high-PUFA margarine and 35 g walnuts (PUFA); 20 g high-MUFA margarine and 45 g almonds (MUFA); 50 g butter (SFA); and 70 g sultanas and 50 g jam (CARB), which provided 25 g PUFA, 26 g MUFA, 27 g SFA, 93 g CARB, and ≈ 1600 kJ per day (Table 1). Fat intake and daily test food checklists were used to assess compliance. Subjects were advised by a research dietitian on how to achieve a low-fat background diet ≈ 20 g per day and to keep their weight stable. A 3-day weighed food record was collected in the second week of each intervention, which included 2 weekdays and 1 weekend day. Subjects were shown how to undertake the weighed food record in a standardized manner by a research dietitian. The dietary data were analyzed using Xyris Diet/1 version 4.2 dietary analysis software (Table 2). Baseline dietary intake was not assessed.

TABLE 2. Dietary Intake Estimated From 3-Day Food Records

	PUFA	MUFA	CARB	SFA
kJ	8355 \pm 1907	8303 \pm 1874	8006 \pm 2137	8420 \pm 1932
% Energy				
Fat	36 \pm 6	37 \pm 7	18 \pm 6	37 \pm 7
PUFA	15 \pm 2*	7 \pm 2	3 \pm 1	4 \pm 1
MUFA	10 \pm 2	19 \pm 3*	6 \pm 3	12 \pm 3
CARB	45 \pm 8	44 \pm 9	65 \pm 9*	45 \pm 9
SFA	9 \pm 3	8 \pm 3	7 \pm 2	19 \pm 4*
Protein	17 \pm 3	18 \pm 3	16 \pm 3	16 \pm 3
Alcohol, g/day	3 \pm 4	2 \pm 4	3 \pm 4	2 \pm 4
Fibre, g/day	31.0 \pm 10.3	31.0 \pm 10.3	30.7 \pm 9.1	27.3 \pm 8.3
Cholesterol, mg/day	174.3 \pm 83.5	206.9 \pm 170.9	167.3 \pm 106.6	326.5 \pm 119.9‡

Data expressed as combined background diet and test food consumption.

Data expressed as means \pm SD; n=40 for each diet.

*Significantly higher compared to all other diets ($P < 0.001$); ‡significantly higher than all other diets ($P < 0.001$).

Ultrasonographic Assessment

Flow-Mediated Dilatation

Subjects underwent assessment of endothelium-dependent FMD of the right brachial artery, as described previously,² after each dietary intervention. Subjects were kept quiet for 5 minutes before FMD measurements, which were taken in the morning after an overnight fast, using a 7.5-MHz linear array transducer of an Acuson Aspen ultrasound (Siemens) before and after forearm ischemia was caused by inflation of a blood pressure cuff to 200 mm Hg for 5 minutes. Measurements were also recorded for 4 minutes at 15-second intervals after a 300- μ g tablet of nitroglycerine was administered sublingually. The operator performing the FMD procedure was blind to the dietary treatment. The coefficient of variation of the computed FMD was 15% (n=6). All FMD measurements were evaluable and none were repeated.

Pulse Wave Velocity

Aortic PWV was measured via Doppler recordings at the carotid and femoral arteries. Approximately 10 consecutive beats were recorded to cover a complete respiratory cycle. A simultaneous ECG recording was used to calculate the interval between the R-wave and the upstroke of each sound wave. The difference between the average intervals for each artery was calculated. PWV was then determined by dividing the measured surface distance by this difference.

Blood Collection

At the end of each intervention, fasting blood samples were collected with Na₂EDTA (final concentration 1 g EDTA/L) for measurement of plasma soluble intercellular adhesion molecule-1 (sICAM-1), soluble vascular cell adhesion molecule-1 (sVCAM-1), and E-selectin, P-selectin, and insulin concentrations, and without Na₂EDTA, for measurement of serum TC, TG, HDL-C, apolipoprotein B (apoB), and high-sensitivity CRP (hs-CRP) concentrations. Plasma and serum samples were isolated with a Beckman GS-6 centrifuge at 2500 rpm for 10 minutes. Aliquots were frozen at -80°C until study completion.

Laboratory Analysis

TC, TG, HDL-C and apoB were measured using a Boehringer Mannheim/Hitachi 902 automatic analyzer. ApoB was measured using a Tina-quant Apolipoprotein B version 2 (Roche Diagnostics). hs-CRP concentrations were measured using a Tina-quant CRP (latex) high-sensitivity kit (Roche Diagnostics). LDL-C concentrations in serum were calculated using the Friedwald equation [(TC-HDL-C)-(TG \times 0.45)]. Concentrations of sICAM-1, sVCAM-1, E-selectin and P-selectin, and insulin in plasma were determined by an ELISA with commercially available kits and standards (ImmunoKontakt; Mercodia Insulin ELISA Enzyme Immunoassay, ALPCO Diagnostics).

Statistics

ANOVA with repeated measures was used. Where ANOVA showed a statistically significant diet effect, pair-wise comparisons using *t* tests and a Bonferroni correction factor were performed. Relationships between variables were determined using linear regression analysis. All analyses were performed using SPSS for Windows 10.0, and statistical significance was set at *P*<0.05. All values are means \pm SD.

Results

Nutritional Analysis, Compliance, and Weight

Good compliance with the intervention diets was achieved as indicated by analysis of weighed food records (Table 2), minimal test foods returned, and dietary checklists. No differences in energy consumption between diets were observed. The desired fat changes were achieved with 2- to 5-fold differences in PUFA, 2- to 2.5-fold differences in SFA,

TABLE 3. Serum Lipid and Insulin Concentrations Following Each Intervention

n=40	PUFA	MUFA	CARB	SFA
HDL-C, mmol/L	1.48 \pm 0.41	1.52 \pm 0.43	1.38 \pm 0.40§	1.56 \pm 0.50
TG, mmol/L	1.32 \pm 0.83	1.33 \pm 0.74	1.71 \pm 1.28*	1.50 \pm 1.06
LDL-C, mmol/L	2.9 \pm 0.99	2.91 \pm 0.85	3.11 \pm 1.00	3.41 \pm 1.13§
TC, mmol/L	4.98 \pm 1.02	4.97 \pm 1.00	5.26 \pm 1.02*	5.65 \pm 1.17*
ApoB, g/L	0.89 \pm 0.22	0.92 \pm 0.60	1.01 \pm 0.39†	1.06 \pm 0.53†
Insulin, mIU/L	6.59 \pm 4.13	7.55 \pm 6.39	7.42 \pm 4.27	7.53 \pm 6.28

Data are expressed as mean \pm SD.

§Different from all other diets; *P*<0.001; *significantly higher than PUFA and MUFA; *P*<0.01; †significantly higher than PUFA and MUFA; *P*<0.001.

n=39 for LDL because 1 subject was excluded because TG >5 mmol/L.

and 2- to 3-fold differences in MUFA (*P*<0.001). Cholesterol intake was highest after SFA compared with all other diets (*P*<0.001). Weight was maintained during the study: PUFA 79.3 \pm 17.3 kg; MUFA 79.0 \pm 17.0 kg; CARB 79.5 \pm 17.9 kg; and SAT 79.5 \pm 17.9 kg.

Lipids, ApoB, and Insulin

TC concentrations (Table 3) were not different comparing PUFA or MUFA but were higher by 5% following CARB (*P* \leq 0.01) and by 13% after SFA (*P* \leq 0.001) compared with PUFA. SFA elevated LDL-C compared with all other diets (*P* \leq 0.005). HDL-C concentrations fell on CARB and were lower than the levels on the high-fat diets (*P*<0.01). The CHO diet also elevated TG by 30% compared with the PUFA and MUFA diets (*P*<0.01). ApoB was significantly higher in the SFA and CARB periods compared with PUFA and MUFA (*P*<0.0001; Table 3).

Insulin

No differences were found in fasting insulin between dietary treatments with or without covariates of HDL and TG (Table 3).

Brachial Artery FMD

Baseline vessel diameter was not different between treatments (4.11 \pm 0.70 mm PUFA; 4.25 \pm 0.64 mm MUFA; 4.06 \pm 0.70 mm CARB; and 4.21 \pm 0.78 SAT). Percentage diameter change after the SFA diet was \approx 50% lower compared with diameter changes after all other diets (*P* \leq 0.001; Figure 1). There was no evidence of carryover from the preceding diet, nor did the SFA diet carryover into subse-

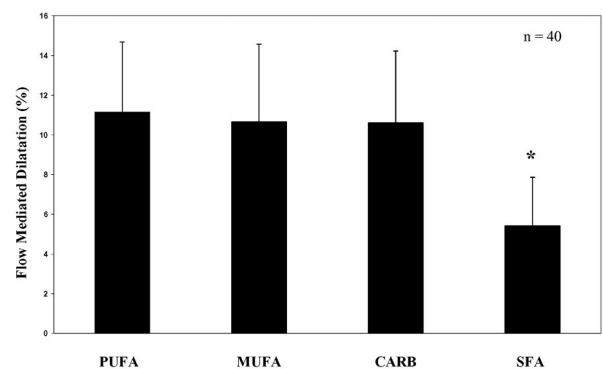


Figure 1. FMD of the brachial artery in response to the diet.

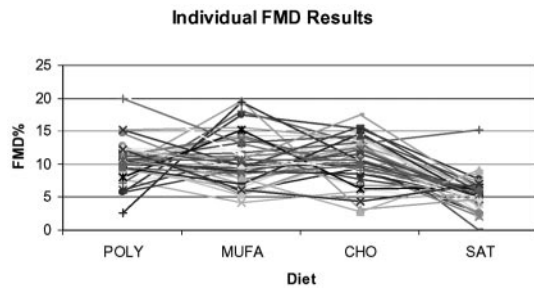


Figure 2. Individual subject results of FMD.

quent diets. The difference from the MUFA period varied from 4.4% to 7.1% with different diet orders ($P=NS$). The FMD-following diets that were low in SFA were very similar to each other (Figure 1). Individual FMD results are presented in Figure 2. GTN-induced dilatation was not different between diets PUFA $17.6\pm 4.0\%$, MUFA $16.8\pm 2.8\%$, CARB $16.9\pm 3.6\%$, and SFA $16.4\pm 4.1\%$ (NS). The data were analyzed to determine whether changes in lipids or apoB had an effect on FMD. Changes in FMD were not related to changes in lipids or apoB, and in this population, FMD was not related to lipid levels in any period. There was no interaction between treatment (drugs/supplements) and FMD response. When those 8 subjects taking blood pressure medication, lipid-lowering agents, or hormone replacement therapy or who smoked were omitted from the analysis, changes in FMD remained significantly different. This remained true when all subjects on either medication or supplements were excluded from the analysis. Age was not related to the change in FMD.

One test to examine carryover effect was performed to examine the effect of a preceding SFA diet on FMD in the next dietary phase regardless of treatment and to compare this with FMD before the SFA phase. The mean FMD was not different after the SFA phase (ie, there was no carryover).

Pulse Wave Velocity

PWV following each diet was related to age ($r=0.4$ to 0.5 ; $P<0.01$) but not to any other variable (Table 4).

Inflammatory Markers

Plasma P-selectin was higher after SFA compared with PUFA ($P=0.002$) and MUFA ($P=0.001$; Figure 3) but not with CARB. Serum hs-CRP and plasma sICAM-1, sVCAM-1, and E-selectin concentrations were not different

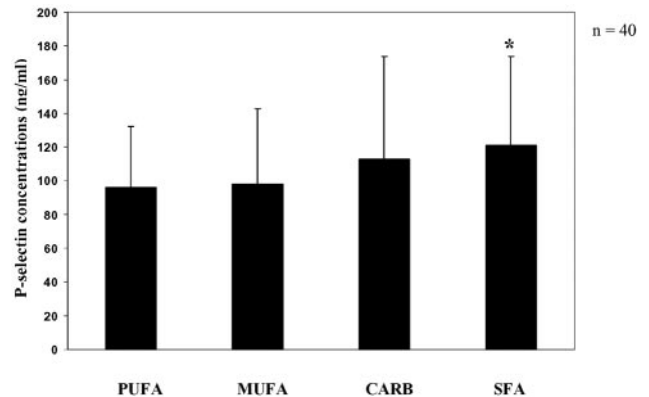


Figure 3. P-selectin levels measured at the end of each dietary phase (mean \pm SD).

between diets (Table 4). There was a positive correlation between CRP and sICAM-1 following SFA ($r=0.463$; $P=0.003$). HDL-C during this phase was negatively related to sICAM-1 and P-selectin ($r=-0.5$, $P=0.001$). No relationship was found between adhesion molecules and FMD response.

Discussion

FMD and Lipid Concentrations

FMD was reduced by 50% following consumption of a high-SFA diet for 3 weeks compared with a high-MUFA or -PUFA diet or a CARB diet. To our knowledge, this has not been reported before following a chronic change in dietary macronutrient composition. Although LDL-C rose during SFA, we did not demonstrate a relationship with this and the deterioration in FMD. ApoB was also higher in the SFA and CARB periods compared with PUFA and MUFA, and similarly, we did not demonstrate a relationship with the deterioration in FMD. Dietary cholesterol was higher during SFA, which would elevate LDL-C to a minor degree during the SFA phase, but it is not possible to separate out the detrimental effects of the fat and cholesterol. No cholesterol-feeding study has examined FMD. Fuentes et al, in a smaller study, demonstrated that FMD was reduced by 27% on a high-SFA diet compared with a MUFA diet (which they attributed to the positive effects of MUFA) but not compared with a low-fat diet, despite similar falls in LDL cholesterol of $\approx 15\%$.¹¹ In our study, in normocholesterolemic subjects, FMD was increased on a low-fat diet relative to a high-SFA

TABLE 4. PWV, Serum CRP, and Plasma Adhesion Molecules After Each Dietary Period

Variable	PUFA	MUFA	CARB	SFA	n
PWV, ms-1	35 \pm 2.77	8.75 \pm 2.10	9.32 \pm 2.31	9.45 \pm 2.74	40
hs-CRP, mg/L	2.44 \pm 1.82	2.46 \pm 2.18	2.56 \pm 1.72	2.91 \pm 2.79	40
sICAM-1, ng/mL	214 \pm 68	238 \pm 80	228 \pm 101	239 \pm 87	40
sVCAM-1, ng/mL	756 \pm 305	748 \pm 235	743 \pm 257	775 \pm 147	40
E-selectin, ng/mL	22 \pm 10	23 \pm 11	23 \pm 13	23 \pm 12	40
P-selectin, ng/ml	96 \pm 36	98 \pm 44	113 \pm 61	121 \pm 53*	40

Data expressed as mean \pm SD; n=40.

*Significantly higher compared with PUFA ($P=0.002$) and MUFA ($P\leq 0.001$).

diet. In cross-sectional studies, high levels of LDL-C and TG-rich lipoproteins inhibit endothelium-dependent vasodilation,^{9,17} but we found in this study, that elevation of TG and lowering of HDL with dietary carbohydrate did not impair endothelial function. Thus, high TG found in subjects normally consuming a relatively high-fat diet is a risk factor for heart disease, but elevation of TG because of carbohydrate appears not to be, at least as assessed by FMD. This is consistent with ecological studies in which Asian countries consuming a CARB diet have higher TG and lower HDL-C levels but substantially lower heart disease rates.^{18,19}

Using a low-fat diet compared with a high-MUFA diet over 24 days, de Roos et al also demonstrated a fall in HDL-C of 0.21 mmol/L and an elevation of TG, whereas LDL remained stable.¹² No effect on FMD was observed, suggesting that reductions in HDL-C with carbohydrate do not adversely affect FMD. Trans fatty acids, which induce falls in HDL cholesterol, caused a deterioration in FMD¹⁴ and are associated with an increase in coronary events.²⁰ In the present study, the high-SFA diet contained some trans in the butter (3% to 5% of fat), and this may have also contributed to the adverse effects. There was no significant trans fat in the other diets.

Ornish et al²¹ demonstrated regression of atherosclerotic lesions on a very low-fat diet despite falls in HDL-C. Ros et al reported improved FMD in hypercholesterolemic subjects after consumption of a high-PUFA diet from walnuts compared with a Mediterranean diet (high MUFA).¹³ In the present study, we found the same FMD after either the high-PUFA or high-MUFA diet. The improvement in FMD observed by Ros et al was associated with a 6.4% reduction in LDL-C on the high-PUFA diet, whereas we did not observe differences in total or LDL-C between MUFA and PUFA. The LDL-C change observed by Ros et al is unexpected given the fatty acid profile of the diet. Walnuts and almonds, which were used in the present study, contain L-arginine, which may enhance NO availability; however, the amounts used in the present study were relatively small, and percent energy from protein was not different between treatments, indicating that dietary L-arginine intakes were not different. The present study was conducted in an outpatient setting with test foods as the source of fatty acids or extra carbohydrate. Compliance with the protocol was demonstrated by the changes in lipids observed, which were consistent with those expected.²² A strength of the present study design was that all subjects underwent all treatments in a randomized design, thus preventing the possible confounding effects of treatment order. Whether the adverse effect of SFA on FMD persists or is even enhanced in the long term is presently unknown.

Adhesion Molecules and FMD

Disturbed endothelial function can also be assessed from levels of adhesion molecules sVCAM1, sICAM1, and E-selectin and P-selectin. It has been postulated that abnormal levels of these molecules are associated with development of atherosclerosis.^{15,23} Levels of sICAM-1 predict future cardiovascular events in healthy subjects.²⁴ The role of P-selectin in the process of atherogenesis has been demonstrated in animal

models, and increased levels of soluble P-selectin in plasma have been observed in coronary artery disease.^{25,26}

In the present study, PUFA and MUFA subjects had lower plasma P-selectin concentrations compared with SFA subjects. Fuentes et al¹⁰ observed a similar finding following a high-MUFA diet and a low-fat diet. They also reported that changes in LDL-C were positively correlated with P-selectin levels and that flow-associated vasodilatation was negatively correlated with P-selectin levels, associations that we did not find.

We observed no differences in plasma CRP, sICAM-1, sVCAM-1, and E-selectin between diets. Brevetti et al showed that subjects with peripheral vascular disease with a low FMD (<6.2%) had higher levels of CRP (6.0 mg/L versus 1.6 mg/L).¹⁶ However, CRP was much lower in our study (2.4 to 2.9 mg/L), and we found no relationship between CRP and FMD. Although weight loss reduces CRP, there have been no interventions showing an effect of dietary fat type or amount on CRP.²⁷ Bemelmans et al found a reduction in SFA intake over 2 years in a dietary intervention study was associated with reduced levels of sICAM-1, which we did not observe in this study.²⁸ In hypercholesterolemic men, there was no significant difference in sICAM-1 or sVCAM-1 concentrations between the SFA diet and the Mediterranean diet, with a similar dietary intervention to our study over 28 days.¹⁰

Lupattelli et al found that subjects with hypertriglyceridemia had raised plasma sICAM-1 and sVCAM-1 concentrations, which were inversely correlated with FMD.²⁹ However, neither sICAM-1 nor sVCAM-1 concentrations in our study were predictors of FMD, nor were they associated with TG levels.

Pulse Wave Velocity

PWV is an independent predictor of cardiovascular mortality, and time to ischemia in coronary artery disease and has been found to relate to FMD and intima medial thickness.^{30–32} Dietary intervention studies using soy and red clover isoflavones have been shown to improve arterial compliance and PWV, with no effect on FMD.^{33,34} However, there are no other dietary intervention studies to date examining the effect of dietary fat changes on PWV.

Conclusions

In this chronic study, we found that SFA impaired endothelial function and that subjects had a marked increase in TG and a fall in HDL-C on the low-fat CARB diet without an effect on FMD. PUFA and MUFA diets compared with SFA reduced P-selectin concentrations. These results lend further support that a high-SFA diet is atherogenic through its adverse effect on endothelial function and P-selectin levels.

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