Changes in plasma lipids and other cardiovascular risk factors during 3 energy-restricted diets differing in total fat and fatty acid composition[1–3]

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ABSTRACT

Background: The well-established relation between changes in dietary fatty acids and plasma lipids has been determined in energy-balance states. Whether this relation is altered in states of energy restriction and active weight loss is not clear.

Objective: The objective of this 12-wk study was to compare the time course of lipid changes and other cardiovascular risk factors in 3 energy-restricted diets (all 6500 kJ) with different total fat and fatty acid compositions.

Design: Sixty-two subjects with a body mass index (in kg/m^2) > 24 were stratified into 1 of 3 parallel dietary intervention groups: *1*) a very-low-fat (VLF) diet (10% of energy from fat; 3% from saturated fat), *2*) a high-saturated-fat (HSF) diet (32% of energy from fat; 17% from saturated fat), and *3*) a high-unsaturated-fat (HUF) diet (32% of energy from fat; 6% from saturated fat).

Results: After 12 wk, LDL cholesterol decreased by 0.66 ± 0.11 ($\bar{x}$ ± SEM) and 0.68 ± 0.12 mmol/L (≈20%) with the VLF and HUF diets, respectively, compared with a decrease of only 0.24 ± 0.11 mmol/L (7%) with the HSF diet ($P < 0.02$ between groups). Diet affected the time course of changes in HDL cholesterol with both high-fat diets, resulting in smaller reductions in HDL cholesterol at weeks 1 ($P = 0.0004$) and 4 ($P = 0.02$); however, these differences were no longer apparent by 12 wk. Overall weight loss was 8.6 ± 0.4 kg (9.7%) and waist circumference decreased by 7.3 ± 5 cm (8%) for the combined groups, with no significant differences between diets.

Conclusions: Significantly greater decreases in LDL cholesterol during active weight loss are achieved with diets low in saturated fatty acids. Changes in HDL cholesterol between diets appear dependent on both the fat content of the diet and the duration of energy restriction. *Am J Clin Nutr* 2000;71:706–12.

KEY WORDS Weight loss, lipids, energy-restricted diet, fatty acids, diet composition, energy restriction, very-low-fat diet, cardiovascular risk factors, humans

INTRODUCTION

The well-established relation between changes in dietary fatty acids and plasma lipid responses has been determined in energy-balance states (1–5). Whether this relation is disturbed in states of energy restriction and active weight loss is not clear. This issue of whether diet composition during weight loss is relevant in lowering cardiovascular risk is important because the prevalence of obesity is increasing and long-term longitudinal studies indicate that obesity independently predicts coronary atherosclerosis (6, 7). One epidemiologic study showed that there is a relation between saturated fat intake and abdominal obesity and hyperinsulinemia (8). This suggests that the macronutrient profile of energy-restricted diets intended for weight loss may modify the reduction in cardiovascular risk.

The relative benefit of weight loss compared with the effect of shifts in dietary macronutrients and fatty acids in lowering cardiovascular risk factors needs clarification, as does the optimum diet composition for weight reduction to lower cardiovascular risk. A meta-analysis of 70 studies (9) on the effect of weight reduction on blood lipids confirmed that weight reduction lowers total and LDL cholesterol and triacylglycerol, whereas an increase in HDL cholesterol depends on whether weight has stabilized. However, it is not clear whether weight loss per se, an energy-restricted diet, or the altered nutrient and fatty acid profiles of the energy-restricted diet is responsible for the improved lipid profile and lower insulin concentrations (10, 11). There is some evidence that each of these factors has separate effects and that the altered fatty acid profile of energy-restricted diets is additive to the effect of weight loss (10).

Our aim was to carry out a clinical trial in humans to evaluate the time course of lipid changes and other cardiovascular risk factors in 3 energy-restricted diets (all containing 6500 kJ) with different total fat and fatty acid compositions in overweight but otherwise healthy subjects. We hypothesized that energy-restricted diets improve the lipid profile consistent with their fatty acid profile and that these effects are additive to the effects of weight loss.

SUBJECTS AND METHODS

Subjects

Seventy-two subjects with a body mass index (BMI; in kg/m^2) > 24 were selected from those recruited by public adver-

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TABLE 1
Baseline characteristics of subjects[1]

	VLF diet (n = 20 W, 2 M)	HSF diet (n = 17 W, 1 M)	HUF diet (n = 22 W, 2 M)
Age (y)	46 ± 2	46 ± 2	45 ± 2
BMI (kg/m^2)	31.1 ± 0.7	31.4 ± 0.6	31.0 ± 0.7
Weight (kg)	85.5 ± 3.0	86.8 ± 2.5	87.3 ± 2.6
Systolic BP (mm Hg)	127 ± 3	128 ± 2	130 ± 3
Diastolic BP (mm Hg)	72 ± 2	75 ± 2	76 ± 2
Fasting glucose (mmol/L)	4.9 ± 0.1[2]	5.2 ± 0.1	5.1 ± 0.1
Total cholesterol (mmol/L)	5.42 ± 0.18	5.73 ± 0.19	5.48 ± 0.19
LDL cholesterol (mmol/L)	3.48 ± 0.19	3.68 ± 0.15	3.44 ± 0.18
HDL cholesterol (mmol/L)	1.16 ± 0.06	1.04 ± 0.05	1.15 ± 0.06
Triacylglycerols (mmol/L)	1.74 ± 0.13	2.25 ± 0.28	1.96 ± 0.18

[1] $\bar{x}$ ± SEM. VLF, very low fat; HSF, high saturated fat; HUF, high unsaturated fat; BP, blood pressure.
[2] Significantly different from HSF diet, $P < 0.01$.

tisement. Subjects who had liver or renal disease, who were taking medication likely to affect lipid metabolism, who consumed >40 g ethanol/d, or who smoked were excluded. Five subjects chose not to commence the study, 3 withdrew because they were noncompliant, and 2 withdrew because of work or travel commitments. Sixty-two subjects (5 men and 57 women) completed the dietary intervention study. Nineteen women were postmenopausal. Approval was obtained from the CSIRO Division of Human Nutrition Human Ethics Committee and informed, written consent was obtained from the volunteers.

Study design

Subjects were blocked into 3 groups and matched for age, sex, BMI, and blood lipid concentrations. Each group took part in one of the following interventions for a total of 12 wk:

1) a very-low-fat (VLF) diet (10% of energy from fat; 3% from saturated fat), *2*) a high saturated fat (HSF) diet (32% of energy from fat; 17% from saturated fat), and *3*) a high unsaturated fat (HUF) diet (32% of energy from fat; 6% from saturated fat).

Fasting blood samples were taken on 2 consecutive days at weeks 0, 1, 4, 8, and 12 and the values at each time point were averaged. Weight and systolic and diastolic blood pressure were also measured at these time points, as were plasma glucose and lipid concentrations (triacylglycerols and total, HDL, and LDL cholesterol).

Blood pressure (Dinamap vital signs monitor 8100; Critikon, Tampa, FL) was measured after subjects had rested quietly for 5 min. Waist measurements were taken before and after dietary intervention. Waist circumference was measured directly on the skin as the smallest dimension between the lower rib margin and the iliac crest. Fasting insulin was measured and an oral-glucose-tolerance test (75 g glucose) was performed at baseline and weeks 1 and 12. Blood samples taken at week 1 of the HSF diet were used as a surrogate measure of the effect of energy restriction on lipid, glucose, and insulin concentrations before any substantial weight loss ($\bar{x}$ ± SEM: −1.45 ± 0.1 kg). During the trial, the need to keep exercise levels at pretrial levels was emphasized.

Age (range: 25–68 y), BMI (25–37), blood pressure (systolic: 100–157 mm Hg; diastolic: 58–97 mm Hg), and plasma lipids (total cholesterol: 3.9–7.5 mmol/L; LDL cholesterol: 2.2–5.6 mmol/L; HDL cholesterol: 0.6–2.2 mmol/L; and triacylglycerol: 0.9–5.7 mmol/L) at baseline were not significantly different between the 3 groups (**Table 1**). The number of postmenopausal women was also not significantly different between groups. There was a physiologically small but statistically significant difference in fasting plasma glucose between the VLF (4.9–5.7 mmol/L) and HSF (4.7–6.2 mmol/L) groups.

Diets

The dietary interventions had the same energy content (6500 kJ) and energy density. This was achieved by providing a set meal plan of identical conventional foods for all 3 diets plus 2 supplementary foods for each of the diets: low-fat biscuits and raisins for the VLF diet, butter shortbread biscuits and milk chocolate for the HSF diet, and canola shortbread biscuits and almonds for the HUF diet. A total of 65% of the energy of the set meal plan was provided to subjects as the supplementary foods and as a wheat-bran breakfast cereal and frozen, low-fat main meals that were the same for all 3 diets. Foods were provided at 2 weekly intervals when subjects visited the research unit for dietary counseling. The subjects purchased all other foods, such as nonfat milk, fruit, vegetables, and bread. Subjects were instructed to not consume alcohol during the trial.

Subjects were counseled by a dietitian on the dietary protocol and on how to keep weighed-food records for nutrient data analysis. Food checklists were completed daily and weighed-food records were completed on 3 d (Sunday, Monday, and Tuesday) every 2 wk. The subjects' weights and diets were monitored every 2 wk by the dietitian and minor dietary adjustments were made on the basis of the rate of weight loss. Information on food preparation was achieved by providing specific recipe information monthly. A total of 18 d of detailed food records was kept for each subject and subsequently analyzed. Nutrient intakes were calculated with DIET/1 NUTRIENT CALCULATION SOFTWARE (Xyris Software, Highgate Hill, Australia), a computer database of foods in which nutrient composition is based on that of Australian foods and that we modified to include data from commercial sources and from an analysis of the supplementary foods. Subjects were also asked to complete a simple numerical satiety rating within 30 min before and after each meal on each day that they completed their food records. The 7-point scale used for satiety rating was as follows: 3, very full; 2, moderately full; 1, slightly full; 0, not hungry and not full; −1, slightly hungry; −2, moderately hungry; and −3, very hungry.

TABLE 2
Nutrient intakes of men and women during the 3 dietary intervention periods, calculated from six 3-d weighed-food diaries[1]

	VLF diet (n = 20 W, 2 M)	HSF diet (n = 17 W, 1 M)	HUF diet (n = 22 W, 2 M)
Energy (MJ)	6.6 ± 0.1[a]	6.4 ± 0.1[a]	6.4 ± 0.1[a]
Protein (% of energy)	18.5 ± 0.3[a]	18.0 ± 0.3[a]	20.5 ± 0.3[b]
Carbohydrate (% of energy)	71.6 ± 0.5[a]	52.1 ± 0.4[b]	48.5 ± 0.5[b]
Fat (% of energy)	10.1 ± 0.3[a]	31.8 ± 0.3[b]	31.8 ± 0.3[b]
Saturated fat (% of energy)	3.3 ± 0.2[a]	16.8 ± 0.2[b]	6.0 ± 0.1[c]
Monounsaturated fat (% of energy)	3.3 ± 0.1[a]	10.0 ± 0.1[b]	16.7 ± 0.2[c]
Polyunsaturated fat (% of energy)	2.1 ± 0.1[a]	2.7 ± 0.1[a]	7.1 ± 0.1[b]
Cholesterol (mg/MJ)	10.9 ± 0.5[a]	23.8 ± 0.5[b]	10.9 ± 0.5[a]
Fiber (g)	38.7 ± 1.2[a]	38.5 ± 1.6[a]	35.4 ± 1.0[a]
Alcohol (g)	0.4 ± 0.3[a]	0.2 ± 0.1[a]	0.2 ± 0.1[a]

[1] $\bar{x}$ ± SEM. VLF, very low fat; HSF, high saturated fat; HUF, high unsaturated fat. Means within rows with different superscript letters are significantly different, $P < 0.01$.

Measurements

Venous blood samples (20 mL) were taken after an overnight fast of ≥ 12 h into tubes containing either trisodium EDTA (final concentration: 1 g/L) as anticoagulant for lipid measurements or sodium fluoride EDTA for glucose measurements. Plasma was separated by low-speed centrifugation at 600 × g for 10 min at 5 °C (GS-6R centrifuge; Beckman, Fullerton, CA) and frozen at −20 °C. At the end of the study, all samples from each subject were analyzed within the same analytic run. Total cholesterol (12), triacylglycerol (13), and plasma glucose concentrations were measured on a Cobas-Bio centrifugal analyzer (Roche Diagnostica, Basel, Switzerland) by using enzymatic kits (Hoffmann-La Roche Diagnostica, Basel, Switzerland) and control sera. Total areas under the glucose curves above baseline during the oral-glucose-tolerance test were calculated geometrically (trapezoidal rule) (14). Plasma HDL-cholesterol concentrations were measured with an HDL Direct kit (Roche Diagnostic Systems, Inc, Somerville, NJ). The following modification of the Friedewald equation (15) for molar concentrations was used to calculate LDL cholesterol in mmol/L: total cholesterol − triacylglycerol/2.18 − HDL cholesterol. Fasting plasma insulin concentrations were determined in duplicate by using a commercial radioimmunoassay kit (Pharmacia AB, Uppsala, Sweden).

Statistical analysis

All data in the text are expressed as means ± SEMs. Repeated-measures analysis of variance was calculated with time as the within-subject factor and diet as the between-subject factor. If the diet-by-time interaction was significant, a comparison of diets at each time point was carried out by using a Bonferroni correction factor. The data were also analyzed to detect endpoint changes with diet by using one-way analysis of covariance with baseline values and weight change as covariates. Multiple stepwise linear regression was used to explore which variables at baseline predicted changes in the key outcome variables. In this case, the change was calculated from a single baseline data point and the other baseline value was used as an independent predictor. The satiety data for each 3-d food record were averaged and analyzed for differences due to study duration, meal times, and diet by using the Kruskal-Wallis H test for independent samples. Analyses were performed with SPSS 8.0 for WINDOWS (SPSS Inc, Chicago). Significance was set at $P < 0.05$.

RESULTS

Dietary intakes showed that the percentage of energy derived from total fat, the fatty acid profile, and the dietary cholesterol composition of the diets were significantly different as expected ($P < 0.001$), whereas the percentages of energy from total fat in the HSF and HUF diets were not significantly different (**Table 2**). Saturated, monounsaturated, and polyunsaturated fatty acids were all significantly higher with the HUF diet than with the VLF diet. There was a small but statistically significant ($P < 0.001$) decrease in energy intake (362 ± 83 kJ) over the course of the study, with no significant difference in changes in energy or macronutrients between diets. Total dietary fiber intakes were high, primarily because of the consumption of the wheat-bran breakfast cereal, which contributed 20 g total dietary fiber but were not significantly different between the diet groups.

Overall weight loss (**Figure 1**) was 8.6 ± 0.4 kg (9.7%), with a reduction in waist circumference of 7.3 ± 5 cm (8%). There were no significant differences in weight loss between diet groups, although weight loss was greatest with the HUF diet (9.5 ± 0.6 kg), next greatest with the HSF diet (8.2 ± 0.7 kg), and least with the VLF diet (7.9 ± 0.9 kg).

Plasma lipid concentrations are summarized in **Table 3**. Because the changes in total cholesterol and LDL cholesterol were similar, only the results for LDL cholesterol are described in detail. There was a powerful effect of time and a strong diet-by-time interaction for LDL cholesterol. Diet composition significantly affected the reduction in LDL cholesterol after 12 wk of the VLF (−0.66 ± 0.11 mmol/L) and HUF (−0.68 ± 0.12 mmol/L) diets, whereas the HSF diet was significantly less effective, resulting in a reduction of only 0.24 ± 0.11 mmol/L ($P < 0.02$ for the between-group comparison of LDL cholesterol at week 12, adjusted for baseline LDL-cholesterol concentrations and weight changes). LDL-cholesterol concentrations were significantly different with the HUF and HSF diets ($P < 0.05$ after Bonferroni correction). The lowest LDL-cholesterol concentration was achieved at 4 wk in response to both the effects of energy restriction and changes from baseline in dietary fat and fatty acids. There were no further changes despite continued weight loss. Although there was no correlation between the change in LDL cholesterol and weight loss at weeks 1, 4, and 8, the correlation was significant by 12 wk, even when adjusted for saturated and unsaturated fatty acid intakes ($r = 0.44$, $P = 0.001$). Whereas LDL cholesterol at week 4 was not correlated with weight loss, it was correlated

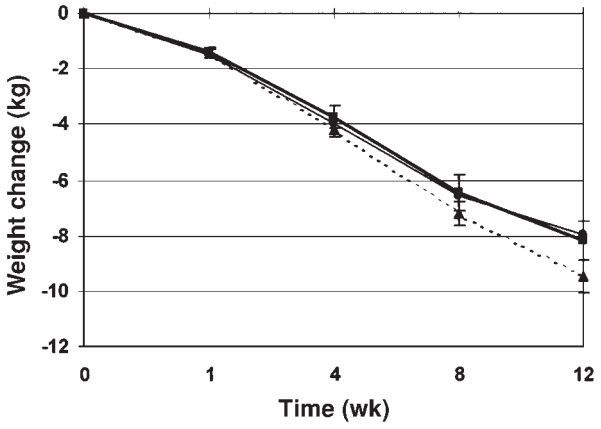

FIGURE 1. Mean (±SEM) weight changes during 12 wk of energy restriction (6500 kJ/d) with 3 different diets: VLF (●), very low fat (n = 22); HSF (■), high saturated fat (n = 18); and HUF (▲), high unsaturated fat (n = 22). There was a significant time effect ($P < 0.001$), but no significant diet-by-time interaction.

with dietary saturated fatty acid intakes (r = 0.27, $P < 0.05$). However, during the subsequent 8 wk, LDL-cholesterol concentrations rose in nearly half the subjects, despite consumption of the same diet and weight loss, suggesting that part of the initial reduction in LDL cholesterol was related to energy restriction, which became relatively less from weeks 4 to 12. The week 12 values thus reflected diet (≈12% of the variance) and weight loss (17% of the variance). In stepwise linear regression analysis, only total weight loss (P = 0.001), initial waist circumference (P = 0.003), LDL cholesterol at baseline (P = 0.002), and absolute intake of saturated fatty acids ($P < 0.001$) predicted the change in LDL cholesterol, together accounting for 47% of the variance. Triacylglycerols fell significantly with time, by 0.36 mmol/L, with no significant effect of diet composition. The change in triacylglycerols at week 12 was highly correlated with baseline triacylglycerols (r = − 0.69, $P < 0.001$). There was a significant fall over time in HDL cholesterol and a time-by-diet interaction (P = 0.009). Although HDL cholesterol at 12 wk was not significantly different from baseline concentrations, diet affected the time course; both the HSF and HUF diets resulted in smaller changes in HDL cholesterol at weeks 1 (P = 0.001 for time-by-diet interaction) and 4 (P = 0.02). HDL cholesterol at weeks 4 and 8 was significantly different from baseline HDL cholesterol (P = 0.002), whereas HDL cholesterol at week 8 was significantly different from that at week 12 (P = 0.003). The ratio of total to HDL cholesterol declined significantly with time, by 0.45 ± 0.19, 0.56 ± 0.24, and 0.79 ± 0.17 with the VLF, HSF, and HUF diets, respectively, but these changes were not significant between diet groups.

Diet composition did not affect glucose tolerance significantly, as measured by the area under the curve for glucose response. The differences in glucose area at the end of the 12-wk intervention were as follows: VLF diet, −0.44 ± 0.74 mmol·h/L; HUF diet, −1.69 ± 0.81 mmol·h/L; and HSF diet, −1.37 ± 0.80 mmol·h/L. Overall glucose tolerance (**Figure 2**) improved significantly at week 1 and this was sustained at week 12 ($P < 0.01$), suggesting that even in nondiabetic subjects, glucose tolerance improves with energy restriction. Furthermore, the difference in glucose area was positively correlated with weight loss (P = 0.02) when baseline glucose concentrations were controlled for, which was also strongly correlated with the change in glucose area ($P < 0.0001$). Fasting plasma insulin (**Figure 3**), which was also unaffected by diet composition, fell significantly with time (−18.2 ± 5.2 pmol/L); this change correlated with the change in glucose area (r = 0.26, P = 0.05).

There was a significant time-by-diet interaction in the reduction in systolic and diastolic blood pressure. The VLF diet group had smaller reductions in both systolic and diastolic blood pressure than the other 2 groups (**Figure 4**). These differences remained significant after adjustment for weight loss.

There were no significant effects of diet on perceived hunger before or after meals, although subjects experienced hunger significantly more before dinner than before other meals ($P < 0.001$). Perceived hunger before dinner decreased significantly with time, less hunger being noted at weeks 8 and 12 than at week 1 (medians: −1.5, −1.3, and –1.0, respectively; $P < 0.05$).

DISCUSSION

We showed that the macronutrient content of energy-restricted diets can have significant effects on plasma lipids during the course of weight loss even when total fat composition approximates the recommended intake of 30% of energy from fat. We observed a differential fall in LDL cholesterol (per kg weight loss) of 0.03 mmol/L with the HSF diet, 0.07 mmol/L with the HUF diet, and 0.08 mmol/L with the VLF diet during active weight loss, indicating that diet composition significantly affected the change in LDL cholesterol during weight loss.

These effects are consistent with the known effects of dietary carbohydrate and fatty acids on the plasma lipoprotein profile in energy-balance states (1–5). This has important implications for the degree of emphasis on the fatty acid profile in weight-loss programs aimed at cardiovascular risk reduction, even when the recommended fat intake is 30% of total energy. The effect of weight loss on LDL cholesterol has been estimated to be a reduction of 0.02 mmol/L per kilogram weight loss (9), but dietary composition was not accounted for in this estimate. In our study, only weight loss at week 12 significantly correlated with the change in LDL cholesterol and accounted for 17% of the variance. Kelley et al (16) found that only 8% of the change in serum lipids was related to weight loss ($\bar{x}$: 40 kg) after gastric bypass surgery, although these patients were likely to still have been in a state of energy restriction and to have diverse dietary intakes. Similarly, Andersen et al (17) reported that weight loss accounted for ≤6% of the variance in total cholesterol reduction in obese women at various stages of weight reduction and maintenance over 48 wk. Dattilo and Kris-Etherton (9), in a meta-analysis of 70 studies, found that weight loss accounted for 9% of the variance in LDL cholesterol. We showed that controlling for the macronutrient composition of the diet clearly affected the variability in the response of LDL cholesterol to weight loss in a manner consistent with what is observed in energy-balance states (1–5).

The effect of diet composition on the decline in HDL cholesterol during weight loss was also in the direction that has been observed in energy-balance studies (2), with higher fat intakes maintaining relatively higher HDL cholesterol than high carbohydrate intakes. Although there was no significant difference in HDL cholesterol between diets or from baseline by week 12, a failure of HDL cholesterol to increase with consumption of a

TABLE 3
Fasting plasma lipids during the 3 dietary interventions[1]

	VLF diet (n = 20 W, 2 M)	Difference from baseline	HSF diet (n = 17 W, 1 M)	Difference from baseline	HUF diet (n = 22 W, 2 M)	Difference from baseline
Total cholesterol (mmol/L)						
Week 0	5.42 ± 0.18	—	5.73 ± 0.19	—	5.48 ± 0.19	—
Week 1	4.94 ± 0.18	—	5.63 ± 0.21	—	4.98 ± 0.20	—
Week 4	4.46 ± 0.21	—	5.18 ± 0.17	—	4.59 ± 0.21	—
Week 8	4.62 ± 0.22	—	5.17 ± 0.15	—	4.53 ± 0.20	—
Week 12	4.62 ± 0.22	−0.80 ± 0.14	5.27 ± 0.16[2]	−0.46 ± 0.20[2]	4.55 ± 0.21	−0.93 ± 0.12
LDL cholesterol (mmol/L)						
Week 0	3.48 ± 0.19	—	3.68 ± 0.15	—	3.44 ± 0.18	—
Week 1	3.20 ± 0.17	—	3.79 ± 0.18	—	3.17 ± 0.18	—
Week 4	2.79 ± 0.19	—	3.39 ± 0.16	—	2.83 ± 0.17	—
Week 8	2.92 ± 0.21	—	3.42 ± 0.15	—	2.78 ± 0.17	—
Week 12	2.82 ± 0.21	−0.66 ± 0.11	3.44 ± 0.15[2]	−0.24 ± 0.11[2]	2.76 ± 0.18	−0.68 ± 0.12
HDL cholesterol (mmol/L)						
Week 0	1.16 ± 0.06	—	1.04 ± 0.05	—	1.15 ± 0.06	—
Week 1	1.06 ± 0.06	−0.10 ± 0.02[3]	1.08 ± 0.05	0.04 ± 0.02	1.13 ± 0.05	−0.03 ± 0.02
Week 4	1.03 ± 0.05	−0.13 ± 0.03[3]	1.04 ± 0.05	0.00 ± 0.03	1.07 ± 0.04	−0.08 ± 0.04
Week 8	1.03 ± 0.05	−0.13 ± 0.04	1.01 ± 0.05	−0.03 ± 0.02	1.08 ± 0.04	−0.07 ± 0.04
Week 12	1.07 ± 0.05	−0.09 ± 0.04	1.06 ± 0.05	0.02 ± 0.02	1.11 ± 0.04	−0.04 ± 0.04
Triacylgycerol (mmol/L)						
Week 0	1.74 ± 0.13	—	2.25 ± 0.28	—	1.96 ± 0.18	—
Week 1	1.51 ± 0.11	—	1.70 ± 0.16	—	1.51 ± 0.14	—
Week 4	1.43 ± 0.09	—	1.67 ± 0.12	—	1.54 ± 0.14	—
Week 8	1.49 ± 0.12	—	1.65 ± 0.14	—	1.49 ± 0.14	—
Week 12	1.60 ± 0.13	−0.14 ± 0.10	1.73 ± 0.12	−0.52 ± 0.26	1.53 ± 0.12	−0.43 ± 0.09
Total:HDL cholesterol						
Week 0	4.93 ± 0.32	—	5.72 ± 0.34	—	5.03 ± 0.32	—
Week 1	4.98 ± 0.37	—	5.39 ± 0.28	—	4.64 ± 0.33	—
Week 4	4.53 ± 0.31	—	5.14 ± 0.26	—	4.43 ± 0.27	—
Week 8	4.71 ± 0.34	—	5.28 ± 0.23	—	4.31 ± 0.25	—
Week 12	4.48 ± 0.29	−0.45 ± 0.19	5.16 ± 0.30	−0.56 ± 0.24	4.24 ± 0.27	−0.79 ± 0.17

[1] $\bar{x}$ ± SEM. There was a significant time effect for all variables, $P < 0.001$. There was a significant diet-by-time interaction for total cholesterol ($P < 0.05$), LDL cholesterol ($P < 0.01$), and HDL cholesterol ($P < 0.01$). VLF, very low fat; HSF, high saturated fat; HUF, high unsaturated fat.
[2] Significantly different from VLF and HUF diets, $P < 0.05$.
[3] Significantly different from HSF and HUF diets, $P < 0.05$.

low-fat diet by subjects whose weight had stabilized was observed previously (9). This latter observation was also made by Nicklas et al (18), who showed that weight loss only partially reversed the HDL cholesterol–lowering effect of an American Heart Association Step I diet. Dattilo and Kris-Etherton (9) predict that for every kilogram decrease in body weight, HDL cholesterol increases by 0.009 mmol/L for subjects at a stabilized, reduced weight and HDL cholesterol decreases by 0.007 mmol/L

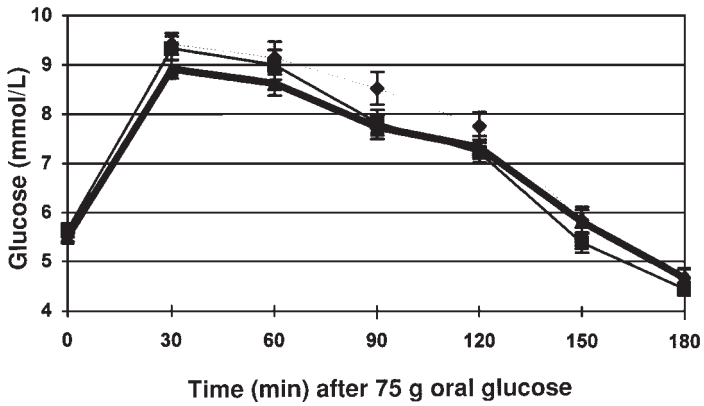

FIGURE 2. Mean (±SEM) glucose responses to a 75-g oral glucose load at weeks 0 (baseline; ◆), 1 (■), and 12 (▲) after weight loss for the 3 diet groups combined: VLF, very low fat (n = 22); HSF, high saturated fat (n = 18); and HUF, high unsaturated fat (n = 22). There was a significant time effect ($P < 0.001$), but no significant diet-by-time interaction.

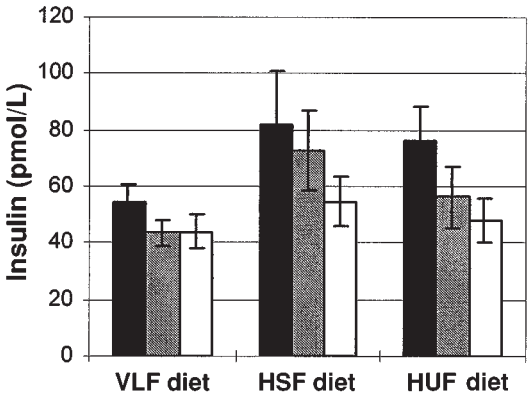

FIGURE 3. Mean (±SEM) fasting plasma insulin concentrations at weeks 0 (baseline; ■), 1 (■), and 12 (□) of energy restriction (6500 kJ) with the 3 different diets: VLF, very low fat (n = 22); HSF, high saturated fat (n = 18); and HUF, high unsaturated fat (n = 22). There was a significant time effect ($P < 0.001$), but no significant diet-by-time interaction.

for subjects actively losing weight. The effect of dietary composition on this relation was not assessed, although one study reported on the effect of stabilized weight loss, independent of diet composition, and found an increase in HDL cholesterol of ≈1% per kilogram of weight lost (11). We showed that a VLF diet exacerbated the decrease in HDL cholesterol during weight loss, although the effect was not sustained over time; therefore, we suggest that the beneficial effect of stabilized weight loss may be attenuated by a VLF diet. This effect may be relevant to the negative effect of weight cycling on morbidity and mortality (19).

The independent effects of weight loss compared with those of dietary fat modification have been elegantly studied by Leenan et al (11), who argued that the favorable effect of weight loss on lipids is greater than that of dietary fat modification. Although this may be true for the substantial 13.5-kg weight loss achieved by this group, resulting in a 0.02-mmol/L decrease in LDL per kilogram of stabilized weight loss, it is not dissimilar to the 0.03-mmol/L decrease we observed in the HSF diet group (control group). However, the effect of dietary fat modification may be greater with smaller weight losses because, in energy-balance studies (2–5), the effect of a change in saturated fatty acid intakes on LDL-cholesterol concentrations suggests that for every 1% reduction in saturated fatty acids there is a corresponding decrease of 0.03–0.04 mmol/L in LDL cholesterol. This is consistent with the differences we observed between the VLF or HUF diet groups and the HSF diet group at weeks 4, 8, and 12, suggesting that the effects of diet composition and weight loss on LDL cholesterol are additive. The expectation that for each 1% reduction in saturated fatty acid intake there is a 0.035-mmol/L decrease in LDL cholesterol would mean a difference in LDL reduction of 0.47 mmol/L [13.5 × 0.035 mmol/L = 0.47 mmol/L (observed: 0.65 − 0.24 mmol/L = 0.41 mmol/L)] between the VLF and HSF diet groups and of 0.38 mmol/L between the HUF and HSF diet groups [10.8 × 0.035 mmol/L = 0.38 mmol/L (observed: 0.69− 0.24 mmol/L = 0.45 mmol/L)]. A realistic reduction in dietary saturated fat of up to 10% of energy, as achieved in this study, may be quantitatively as effective at lowering LDL cholesterol as would be a 20-kg weight loss without a reduction in saturated fatty acid intake. Because even modest weight losses of ≈5–10% of initial body weight are associated with beneficial effects on cardiovascular risk factors (20) and increased longevity in women with comorbidities (21), successful management of obesity has been redefined so that more achievable weight losses are achieved. This suggests that an appropriate dietary fatty acid profile of weight-loss diets should be emphasized to achieve optimum lipid lowering and hence cardiovascular risk reduction.

No significant differences were seen in glycemic control between the diet groups, but substantial reductions in fasting glucose and insulin and plasma glucose after a 75-g glucose load were observed as early as 7 d of consumption of all 3 energy-restricted diets. Studies have shown no significant difference in insulin sensitivity between diets that differ within practicably achievable fat intakes in nonobese subjects (22, 23).

The observation that the VLF diet was least effective in lowering blood pressure during weight loss was unexpected. Some (24–27) but not all (28) studies have noted no significant differences in blood pressure between low-fat and high-monounsaturated-fat diet groups in weight-stable or energy-restricted (24) dietary interventions.

In conclusion, we showed that, overall, energy-restricted diets improve cardiovascular risk factors in obese subjects during active weight loss. However, the macronutrient and fatty acid composition of the energy-restricted diet can exert substantial

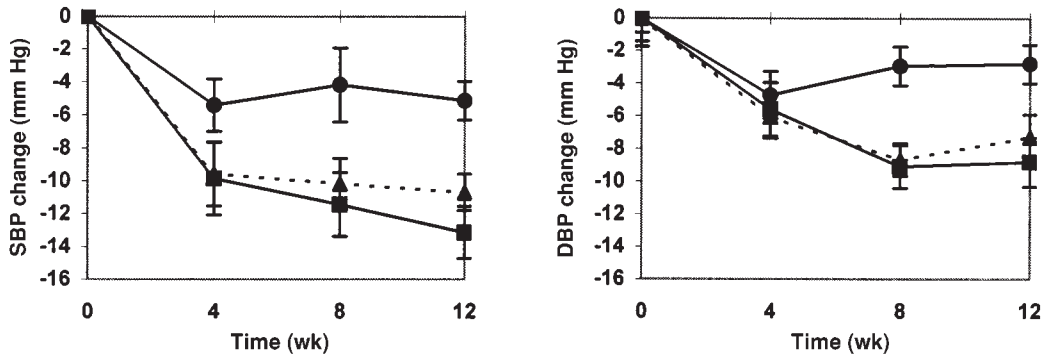

FIGURE 4. Mean (±SEM) changes in systolic (SBP) and diastolic (DBP) blood pressure during 12 wk of energy restriction (6500 kJ) with the 3 different diets: VLF (●), very low fat (n = 22); HSF (■), high saturated fat (n = 18); and HUF (▲), high unsaturated fat (n = 22). There was a significant time effect ($P < 0.001$) and a significant diet-by-time interaction ($P = 0.006$).

effects, even when such diets approximate currently recommended total fat intakes. The observed changes in lipoprotein profile were consistent with changes observed in energy-balance studies. Our data suggest that dietary recommendations for weight loss to lower cardiovascular risk should consider a shift in emphasis from total fat restriction to saturated fat restriction.

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