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Baseline inflammatory markers do not modulate the lipid response to weight loss

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Abstract

Recent studies have found that baseline inflammatory status affected the response of the lipid profile to diet intervention. The goal of this study was to determine whether baseline inflammatory status, as reflected in C-reactive protein, interleukin 6, and tumor necrosis factor α, affected the lipid and insulin response to a weight loss intervention. A second goal was to determine whether inflammatory markers were related to traditional metabolic risk factors, such as lipids and insulin, in our sample of 190 overweight (body mass index, 27-30 kg/m^2) premenopausal women. Body composition, fat distribution, serum lipids, insulin sensitivity (Si), and markers of inflammation were assessed at baseline and after weight loss to body mass index <25 kg/m^2. All measurements were taken after a 4-week period of weight maintenance. Mixed-model, repeated-measures analysis was used to determine whether the interaction of baseline inflammatory status and time was significant in determining the changes in metabolic risk factors (Si and lipids) with weight loss. Weight loss was associated with significant reductions in total cholesterol, low-density lipoprotein cholesterol, triglycerides, and insulin, and increases in high-density lipoprotein cholesterol and Si. Triglycerides were higher (P = .054) and Si lower (P = .057) with increasing C-reactive protein tertile. The interaction of baseline inflammatory status and time was not significant for any outcome variable of interest. These results do not support the hypothesis that baseline inflammatory status affects the lipid and insulin response to a weight loss intervention. However, in these young, healthy women, weight loss had a beneficial impact on both inflammatory status and risk factors for chronic metabolic disease.

1. Introduction

Chronic inflammation is increasingly being recognized as a risk for cardiovascular disease (CVD) [1-3] and type 2 diabetes mellitus [4-6]. Particularly, proinflammatory cytokines have been reported to induce the production of interleukin 6 (IL-6), which in turn stimulates the production of C-reactive protein (CRP) from the liver. High circulating levels of CRP would then increase the concentration of circulating cell adhesion molecules and tissue factors as well as mediate the uptake, by macrophages, of low-density lipoprotein cholesterol (LDL-C) [1], leading to atherosclerotic plaque. C-reactive protein can thus be considered a major risk factor in the progression of CVD and has been recognized as an emerging risk factor by the National Cholesterol Education Program Adult Treatment Panel III [7].

However, markers of inflammation also may more broadly reflect metabolic status. In diet intervention studies, baseline CRP concentration was associated with the nature and degree of diet-induced changes in triglycerides (TG) [8]. For example, men with low CRP concentrations at baseline had a reduction in fasting TG whereas those with high baseline CRP had an increase in TG with a low-fat diet. With a high–monounsaturated fat diet, men with high CRP had greater reductions in total cholesterol (TC) and LDL-C than those with low baseline CRP. Similar interactive relationships between CRP and diet on lipids have been reported [9-11].

Previous studies have thus shown that an individual's lipid response to dietary treatment may be dependent on his/her CRP levels at diet onset. We therefore designed this study to determine if the lipid and insulin responses to a weight

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loss intervention would differ depending on baseline inflammatory status. The objective of this study was to examine whether baseline inflammatory status would modulate the effects of a weight loss intervention on CVD risk factors in overweight, premenopausal women. We hypothesized that subjects with high baseline levels of inflammatory markers would have greater reductions in lipid levels and a greater improvement in insulin sensitivity (Si) than subjects with low baseline levels of inflammatory markers. A second objective of this study was to examine the association between inflammatory markers and traditional metabolic risk factors, such as lipids and insulin, in overweight women. We hypothesized that women who had higher insulin and lipid levels would also have higher levels of inflammatory markers.

2. Subjects and methods

Subjects included 213 black and white premenopausal women between the ages of 20 and 41 years recruited for a weight loss intervention study designed to examine the long-term effects of exercise on weight loss and body composition. Subjects were recruited at a body mass index (BMI, in kilograms per square meter) of 27 to 30 and had a family history of overweight (BMI >27) in at least one first-degree relative. Classification of black or white included subjects' report that both parents and grandparents were of that race. Normal glucose tolerance was documented by an oral glucose tolerance test. Subjects were nonsmokers and were not taking medications known to affect energy expenditure, fuel utilization, insulin concentration, heart rate, or thyroid status. The study was approved by the University of Alabama at Birmingham Institutional Review Board.

Before testing, subjects underwent a 4-week outpatient energy balance period, during which body weight was measured at the General Clinical Research Center (GCRC) 3 times weekly during the first 2 weeks and 5 times weekly during the final 2 weeks. Throughout this period, the energy content of the meals was adjusted to achieve energy balance. At the end of the 4-week period, subjects were admitted to the GCRC for testing. Testing included a frequently sampled intravenous glucose tolerance test for determination of Si; blood sampling in the fasting state for determination of fasting lipids, glucose, and inflammatory markers; and body composition measurements (anthropometrics, dual-energy x-ray absorptiometry [DXA], and computed tomography [CT]). Details of the measurement methods are given below.

After the 4-week energy balance period, subjects were randomized to 3 weight loss groups: (1) weight loss by diet alone, (2) weight loss by diet and aerobic exercise, and (3) weight loss by diet and resistance exercise. Subjects assigned to the exercise groups participated in 3 supervised training sessions per week throughout the active weight loss phase. The active weight loss period ended when the subject had achieved a BMI of <25.

At the end of the active weight loss period, subjects were again placed on a 4-week energy balance period. Baseline measurements were repeated at the end of this post–weight loss energy balance period. Subjects assigned to the exercise groups continued to participate in the exercise sessions throughout this period. The subjects included in this study are those who successfully lost >10 kg and reached a BMI of <25.

2.1. Body composition measurements

Body composition was assessed by DXA and CT scanning. A whole-body DXA scan (Prodigy; GE-Lunar, Madison, WI) was performed at baseline and after weight loss. Intraabdominal adipose tissue (IAAT) was assessed via CT scanning at the level of the L4−L5 vertebrae. The CT scans were performed at baseline and after weight loss using a HiLight/HTD Advantage scanner (General Electric, Milwaukee, WI). The scanner was set at 120 peak kV and 40 mA, as previously described [12]. All scans were read by the same trained research assistant.

2.2. Collection of sera and frequently sampled intravenous glucose tolerance test

At approximately 7:00 AM, after a 12-hour fast, flexible intravenous catheters were placed in the subject's antecubital spaces of both arms. Three blood samples were drawn over a 40-minute period, and sera were subsequently separated and pooled for analysis of lipids and markers of inflammation. Three additional blood samples were taken over a 20-minute period for determination of basal glucose and insulin (the average of the values was used for basal "fasting" concentrations). At time 0, glucose (50% dextrose, 11.4 g/m^2) was administered intravenously. At minute 20 after glucose administration, subjects received an intravenous bolus of insulin (0.02 U/kg). Blood samples were collected at the following times relative to glucose administration at 0 minute: 2, 3, 4, 5, 6, 8, 10, 12, 15, 19, 20, 21, 22, 24, 26, 28, 30, 35, 40, 45, 50, 55, 60, 70, 80, 100, 120, 140, 180, 210, and 240 minutes. Sera were analyzed for glucose and insulin, and values were entered into the MINMOD computer program (Version 3.0; copyright, Richard N Bergman) for determination of Si and the acute insulin response to glucose (AIR_g) [13-15]. The AIR_g is the integrated incremental area under the curve for insulin during the first 10 minutes of the test.

2.3. Assay of glucose, insulin, and lipids

Analyses were performed in the Core Laboratory of the GCRC and the Clinical Nutrition Research Center at the University of Alabama at Birmingham. Glucose was measured in 10-μL sera using an Ektachem DT II System (Johnson and Johnson Clinical Diagnostics, Rochester, NY). In the Core Laboratory, this analysis has a mean intraassay coefficient of variation (CV) of 0.61% and a mean interassay CV of 1.45%. Insulin was assayed in duplicate 100-μL aliquots with Linco Research Products (St Charles, MO) reagents. In the Core Laboratory, this assay has a sensitivity of 3.35 μIU/mL, a mean intraassay CV of 3.49%, and a mean interassay CV of 5.57%. Commercial-quality control sera of low, medium, and high insulin concentration are included in every assay to monitor variation over time. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), and TG were measured with the Ektachem DT II System. With this system, HDL-C is measured after precipitation of LDL-C and very low-density lipoprotein cholesterol with dextran sulfate and magnesium chloride. Control sera of low and high substrate concentration are analyzed with each group of samples, and values for these controls must fall within accepted ranges before samples are analyzed. The DT II is calibrated every 6 months with reagents supplied by the manufacturer. The LDL-C was estimated using the Friedewald formula [16].

2.4. Assays of markers of inflammation

All markers of inflammation were assessed using enzyme-linked immunosorbent assays (ELISAs). Tumor necrosis factor (TNF) α was assessed using a high-sensitivity ELISA kit (Quantikine HSTA00C; R and D Systems, Minneapolis, MN). This assay requires 200 μL sera per test. Sensitivity is 0.5 pg/mL, mean intraassay CV is 9.0%, and mean interassay CV is 19.0%. The IL-6 was assayed using the Quantikine HS600B (R and D Systems). This assay requires 100 μL sera per test. Sensitivity is 0.156 pg/mL, mean intraassay CV is 12%, and mean interassay CV is 14.5%. The CRP was assayed using the high-sensitivity ELISA kit 030-9710s (ALPCO, Windham, NH). The CRP samples were diluted in a 1:100 ratio before analysis. This assay requires 100 μL diluted sera per test (sera diluted 1:100). Sensitivity is 0.124 ng/mL, mean intraassay CV is 13%, and mean interassay CV is 12.6%.

2.5. Statistical methods

Baseline characteristics are presented as means and standard deviations. Distributions of TG, AIR_g, Si, and insulin were skewed and were transformed to the log10 scale for analysis. To evaluate the relationship between baseline inflammatory markers (CRP, IL-6, TNF-α) and the lipid and insulin outcome variables, the inflammatory markers were divided into clinically relevant categories. The CRP was categorized as <1.0, 1.0 to 3.0, or >3.0 mg/L as described by the Centers for Disease Control and Prevention and the American Heart Association [17]. Because there is no established guideline for risk assessment cut points for IL-6 and TNF-α, baseline concentrations were analyzed both as continuous and as categorical variables. As categorical variables, IL-6 and TNF-α were divided into tertiles: ≤1.16, 1.17 to 1.7, and >1.7 pg/mL for IL-6 and ≤0.5, 0.51 to 0.85, and >0.85 pg/mL for TNF-α. Results for IL-6 and TNF-α were similar whether data were analyzed as continuous or categorical. Thus, results were presented as categorical to be consistent with those for CRP.

In all analyses, women with CRP levels of >10.0 mg/L were excluded (n = 16) as suggested by the Centers for Disease Control and Prevention and the American Heart Association because such high CRP levels may represent acute inflammation or infection [17]. Seven women in the 2 exercise intervention groups were excluded because they were less than 70% adherent to their regimens. Therefore, 190 subjects are included in this investigation.

Relationships between baseline inflammatory marker concentrations and lipid and insulin concentrations were examined by the MIXED procedure in SAS (Version 9.1; SAS Institute, Cary, NC) for repeated measurements, with adjustment for changes in IAAT and controlling for time (before or after weight loss measurement period), race (white vs black), and baseline age in years. Predicted mean concentrations of lipids and fasting insulin and Si were plotted by level of baseline inflammatory marker. Mean levels across categories were compared using the Tukey adjustment. Baseline inflammatory marker × visit interactions were tested in each multivariate model. These interactions of inflammatory marker on lipids, glucose, and insulin variables were our main outcomes of interest. The impact of race on these interactions was tested but was found to be not significant. All relationships were considered significant at $P < .05$.

3. Results

There was no difference between treatment groups in weight, BMI, waist circumference, lipid parameters, glucose, insulin, AIR_g, Si, and markers of inflammation across the weight loss period. Consequently, treatment groups were combined for subsequent analyses. Table 1 shows the anthropometric characteristics of the subjects before and after weight loss as well as their serum concentrations of lipids and markers of inflammation. Per study protocol, all women lost weight and had reductions in BMI, waist circumference, and body fat during the study. With the exception of HDL-C, which increased, all plasma lipid parameters decreased as well as AIR_g, fasting insulin, and IL-6 concentrations. Insulin sensitivity was increased after weight loss.

Regression models testing the relationship between baseline concentrations of inflammatory markers and lipid and insulin responses to weight loss are shown in Tables 2, 3, and 4. The baseline CRP × time interaction was not significant for any dependent variable (TC, LDL-C, HDL-C, TG, fasting insulin, or Si). Baseline CRP concentration was not a significant predictor of any dependent variable examined, but there was a trend toward significance for TG ($P = .0549$, Fig. 1) and Si ($P = .0573$, Fig. 1B). Women in the

Table 1
Anthropometric characteristics, serum lipids, and cytokines in women before and after weight loss (n = 190)

	Overweight	Weight reduced	*P* for overweight vs weight reduced
Body weight (kg)	76.5 (7.1)	65.1 (6.3)	<.0001
BMI (kg/m^2)	28.3 (1.4)	23.9 (1.0)	<.0001
Waist circumference (cm)	86.9 (6.6)	75.9 (5.1)	<.0001
Total body fat (%)	44.8 (4.0)	34.4 (5.1)	<.0001
IAAT (cm^2)	79.6 (32.1)	48.9 (21.7)	<.0001
TC (mg/dL)	157.2 (31.9)	151.0 (27.8)	.005
LDL-C (mg/dL)	99.5 (29.2)	92.5 (23.8)	<.0001
HDL-C (mg/dL)	39.7 (10.5)	45.0 (11.8)	<.0001
TG (mg/dL) [a]	89.3 (40.6)	67.7 (27.0)	<.0001
Fasting glucose (mg/dL)	87.5 (6.7)	86.3 (7.3)	.29
Fasting insulin (μIU/mL) [a]	11.8 (4.0)	8.4 (3.3)	<.0001
AIR$_g$ (μIU/mL × 10 min)	777.1 (544.4)	580.2 (437.2)	<.0001
Si^3 (μIU/mL × 10^{-4} min^{-1})	3.0 (1.8)	4.6 (2.2)	<.0001
CRP (mg/L)	2.1 (1.9)	1.9 (6.2)	<.0001
IL-6 (pg/mL) [a]	1.7 (1.2)	1.3 (0.8)	.001
TNF-α (pg/mL)	1.10 (2.44)	0.94 (0.75)	.06

Values are means (SD).
[a] Statistical analyses were performed on log-transformed values.

highest CRP category had higher TG concentrations than those in the lowest CRP group ($P < .05$), and women in the lowest CRP group had higher Si than those in the highest CRP group ($P < .05$).

Similarly for IL-6 (Table 3), the baseline IL-6 × time interaction was not significant for any dependent variable. Finally, the baseline TNF-α × time interaction was not significant for any dependent variable (Table 4).

4. Discussion

Results of this study showed that the changes in serum lipid concentrations and Si with weight loss did not vary depending on the subject's baseline inflammatory status. Results also showed that inflammatory status was associated with traditional cardiovascular and diabetes risk factors. Individuals with higher markers of inflammation also had a less desirable lipid profile and lower Si. In fact, for all 3 inflammatory markers studied, CRP, IL-6, and TNF-α, the metabolic risk factors were more adverse in individuals with higher inflammatory status than in those in the lowest tertile of inflammation. Insulin sensitivity was lower in individuals in the highest tertile of CRP and IL-6, whereas TG was higher in women in the 2 higher tertiles of CRP.

Heliovaara et al [18] have previously shown that, in normal-weight men and women, Si is inversely associated with IL-6 but did not find the association, as we have, with CRP. Piche et al [19] also found that postmenopausal women in the highest CRP tertile (≥3.0 mg/L) had higher TG and lower Si than women in the lowest tertile (<1.0 mg/L). However, unlike our results, they found that differences in TG between CRP tertiles disappeared after adjustment for IAAT. Differences in Si were maintained. Differences between those results and ours with regard to differences in TG with increasing CRP levels may be due to the larger variability in IAAT in their cohort and higher IAAT levels in their postmenopausal women relative to our premenopausal women. Intraabdominal adipose tissue may be a more important modulator of lipoproteins at higher levels of IAAT than at lower levels. Piche et al [19] concluded that CRP levels had no independent effect on plasma lipoproteins. Based on our data, it may be necessary to specify that this may be the case only in postmenopausal women or in women

Table 2
Relationship between change in plasma lipids and baseline CRP levels during weight loss

Factor	TC		LDL-C		HDL-C		TG (log10)		Insulin (log10)		Si (log10)	
	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*
Age (y)	.7460		.5368		.1100		.0027		–.0035		.0087	.0009
	(.3729)	.0468	(.3414)	.1176	(.1264)	.3855	(.0002)	.1338	(.0018)	.0518	(.0026)	
IAAT	.0576	.3614	.0603	.2679	–.0471	.0393	.001	.0040	.0012	.0012	–.0026	<.0001
	(.0629)		(.0538)		(.0227)		(.0004)		(.0004)		(.0005)	
Baseline CRP (mg/L)												
<1	.0		.0		.0		.0		.0		.0	.0573
1-3	9.4315	.4097	7.4770	.4100	–3.4807	.3985	.1247	.0549	.03476	.1778	.0352	
	(7.5335)		(6.4830)		(2.7894)		(.0527)		(.0551)		(.0847)	
>3	8.7315		8.5566		–3.4226		.0969		.1204		–.2335	
	(8.8797)		(7.6266)		(3.2949)		(.0624)		(.0648)		(.1002)	
Race (White vs Black)	6.6353	.1673	4.3868	.2947	–3.8676	.0137	.1461	–.0001	–.0487	.0280	.2185	<.0001
	(4.5714)		(4.1751)		(1.5543)		(.0225)		(.0220)		(.0317)	
Visit	–4.1992		–4.0074		2.0481		–.0601		–.0794		.0987	<.0001
	(4.0171)	.0482	(3.3423)	.0327	(1.5338)	.0033	(.0298)	<.0001	(.0312)	<.0001	(.0474)	
Baseline CRP (mg/L) * visit	.0		.0		.0		.0		.0		.0	.4255
<1	–4.5970		–3.6591		2.4321		–.0718		–.0204		.0149	
1-3	(4.6711)	.5832	(3.8121)	.5994	(1.8282)	.4140	(.0377)	.1595	(.039)	.3599	(.0616)	
	–.5982		–.4942		1.4910		–.0234		–.0686		.0949	
>3	(5.7058)		4.6610)		(2.2302)		(.0457)		(.0479)		(.0745)	

Table 3
Relationship between change in plasma lipids and baseline IL-6 tertiles during weight loss

Factor	TC		LDL-C		HDL-C		TG (log10)		Insulin (log10)		Si (log10)	
	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*	β (SE)	*p*	β (SE)	*P*	β (SE)	*P*
Age (y)	.7471	.0489	.5038	.1459	.1504	.2277	.0026	.1699	−.0036	.0436	.0092	.0006
	(.3769)		(.3451)		(.1242)		(.0019)		(.0018)		(.0026)	
IAAT	.0772	.2253	.0676	.2201	−.0378	.0984	.0011	.0031	.0011	.0034	−.0024	<.0001
	(.0634)		(.0549)		(.0228)		(.0004)		(.0003)		(.0005)	
Baseline IL-6 (pg/mL)	.0		.0		.0		.0		.0		.0	.0647
≤1.16	.0884		1.0305		−3.9776		.04407		.0311		−.1850	
1.17-1.7	(8.0199)	.9153	(6.9239)	.4528	(2.9889)	.4141	(.0561)	.1292	(.0593)	.6789	(.0902)	
	3.0309		8.1871		−2.0212		−.0723		.0523		−.829	
>1.7	(8.0648)		(6.9768)		(2.9984)		(.0563)		(.0598)		(.0902)	
Race (White vs Black)	5.5457	.2299	3.7329	.3757	−3.9937	.0095	.1444	<.0001	−.0456	.0362	.2201	<.0001
	(4.6050)		(4.2044)		(1.5249)		(.0230)		(.0221)		(.0326)	
Visit	−2.7972		−3.5108		4.2739		−.0976		−.0961		.0674	<.0001
	(4.1007)	.0511	(3.4383)	.0280	(1.5831)	.0015	(.0302)	<.0001	(.3236)	<.0001	(.0491)	
Baseline IL-6 (pg/mL) ∗ visit												
≤1.16	.0		.0		.0		.0		.0		.0	.1919
1.17-1.7	−5.0884		−2.1198		−.4114		−.0365		.0021		.1051	
	(5.0458)	.5689	(4.1542)	.6353	(2.0151)	.6996	(.0403)	.1321	(.0435)	.6550	(.0662)	
>1.7	−3.8249		−3.8658		−1.6321		.0475		−.0340		.1032	
	(4.9417)		(4.0595)		(1.9830)		(.0400)		(.0435)		(.0655)	

with high IAAT. This is supported by findings from another group who found, as we did, a negative association between IL-6, CRP, and Si [20]. This group also reported that, in their population of overweight men and women, Si was the strongest predictor of CRP and IL-6, above and beyond the role percentage of body fat plays on Si.

No previous study has examined the role of pre–weight loss inflammatory status on the lipid response to weight loss. Several studies have looked at the association between baseline inflammatory status and the response to diet composition [8-11]. Zhao et al [10] reported a 29% lower cholesterol-lowering response to high–polyunsaturated fat diets in subjects with elevated CRP concentrations relative to those with lower CRP levels. These data differ from those of Desroches et al [8] who found greater reductions in TC and LDL-C with consumption of a high–monounsaturated fat diet by subjects with high baseline CRP concentrations than those with lower CRP concentrations at baseline. However, TG reductions were greater in subjects with low baseline CRP relative to high-CRP subjects. Furthermore, those with higher baseline CRP had increases in TG when placed on a low-fat diet, whereas those with low CRP at baseline had a

Table 4
Relationship between change in plasma lipids and baseline TNF-α tertiles during weight loss

Factor	TC		LDL-C		HDL-C		TG (log10)		Insulin (log10)		Si (log10)	
	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*	β (SE)	*P*
	.8577	.0214	.6108	.0743	.1372	.2722	.00028	.1242	−.0036	.0423	.0086	.0017
Age (y)	(.3697)		(.3404)		(.1246)		(.0018)		(.0019)		(.0027)	
Visceral fat	.0497	.4249	.0604	.2644	−.0528	.0208	.0011	.0054	.0012	.0017	−.0026	<.0001
	(.0622)		(.0539)		(.0227)		(.0003)		(.0003)		(.0005)	
Baseline TNF-α (pg/mL)												
≤.5	.0		.0		.0		.0		.0		.0	.6344
0.51-0.85	4.3115		8.4714		−2.2228		−.0206		.0494		−.0625	
	(7.8128)	.4510	(6.7653)	.3221	(2.9368)	.4171	(.0558)	.6822	(.0575)	.2320	(.0898)	
>0.85	10.3812		9.4952		1.8654		.0309		.1040		.0227	
	(8.2160)		(7.0947)		(3.0975)		(.0587)		(.0606)		(.0929)	
Race (White vs Black)	4.7067	.3071	2.5092	.5532	−3.4580	.0271	.1383	<.0001	−.0449	.0459	.2262	<.0001
	(4.5967)		(4.2242)		(1.5534)		(.0233)		(.0223)		(.0332)	
Visit	−6.2729	.0375	−4.8691	.0320	3.7324	.0056	−.1079	<.0001	−.0578	<.0001	.2262	.0002
	(4.0310)		(3.3617)		(1.5774)		(.0308)		(.0316)		(.0333)	
Baseline TNF-α (pg/mL) ∗ visit												
≤0.5	.0		.0		.0		.0		.0		.0	.5711
0.51-0.85	−2.8457		−3.6444		−1.0745		.0335		−.0630		.0354	
	(4.7778)	.5034	(3.9046)	.3698	(1.9301)	.8537	(.0397)	.6415	(.0415)	.1216	(.0648)	
>0.85	3.2680		2.2320		−.6890		.0005		−.0865		−.0378	
	(5.1836)		(4.2416)		(2.0877)		(.0425)		(.0445)		(.0685)	

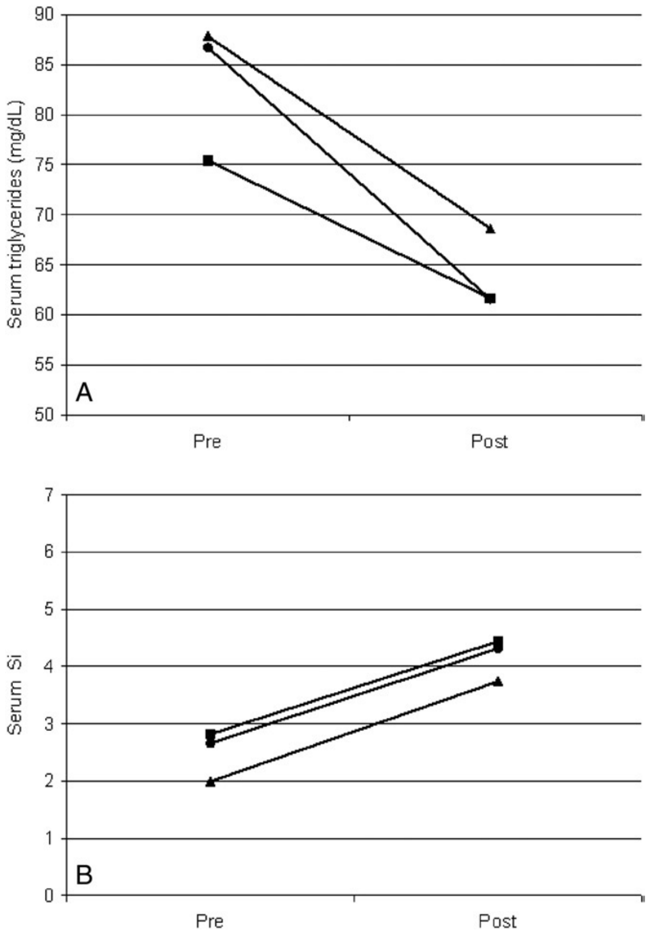

Fig. 1. Changes in plasma TG (A) and Si (B) induced by weight loss stratified by baseline CRP levels (squares = CRP <1, circles = CRP 1 to 3, triangles = CRP >3 mg/L). Values are predicted means controlling for changes in visceral fat, race, age, and visit. A, $P < .05$ for CRP <1 vs 1 to 3 mg/L. B, $P < .05$ for CRP <1 and 1 to 3 vs >3 mg/L.

reduction in TG. These results are in accordance with those of Hilpert et al [9] who also found that subjects with high CRP levels had increases in atherogenic risk factors when placed on a low-fat diet, whereas those with low CRP had reductions in risk. Improvements in TC and LDL-C were also found to be greater in subjects with low relative to high baseline CRP when placed on the Dietary Approaches to Stop Hypertension diet [11].

In light of the studies described above, we had hypothesized that lipid responses to weight loss would differ based on the subject's baseline inflammatory status. We did not find such interaction of inflammatory status by weight loss on the metabolic risk variables studied. However, we may have needed a larger sample size to detect the impact of baseline CRP levels on TG and Si, which showed a trend for an effect in our study. In our study, few women had elevated CRP levels at baseline, with only 23.1% having CRP >3 mg/dL. Perhaps an effect of baseline CRP on changes in TG and Si with weight loss would have been detected if our sample had more heterogeneous baseline CRP levels.

There are some unique and important aspects to this study that deserve mention. First, a similar number of black and white women participated in this study, allowing us to examine potential racial differences in outcomes of interest. Second, women were in energy balance during both measurement periods; and the foods they consumed during those periods were identical. Thus, our results were not affected by the subjects' food choices and energy status.

This study also has several limitations. First, only premenopausal women were included. It is therefore unknown whether similar results would apply to postmenopausal women and men. Race and sex differences have been found in CRP [21]. A report by our group showed that nitrate and nitrite levels are different between black and white women at similar body weight and that myeloperoxidase levels change in opposite directions in response to weight loss in black and white women [22]. One study examining sex differences in correlations between different CVD risk factors reported more and stronger correlations in female than male subjects [23].

Second, only healthy women were included in this study; and all were within a narrow BMI range of 27 to 30. It is possible that different results would be observed if our sample had been more heterogeneous in health and BMI status. The men in the study by Desroches et al [8], for example, had a wider range of BMI than the women in our study and the authors found that baseline CRP concentrations influenced the lipid responses to diets. Similarly, subjects in the study by Hilpert et al [9] and by Zhao et al [10] had a wider range of BMI and higher plasma lipid concentrations than the women in this study.

In conclusion, this study did not find that inflammatory status was related to the lipid and insulin response to a weight loss program in otherwise healthy, overweight women. More research is necessary to determine whether similar results would be obtained in subjects at risk for CVD and diabetes. However, our data confirm previous findings that individuals with elevated markers of inflammation also have other elevated risk factors for CVD and diabetes, even in moderately overweight, otherwise healthy young women.

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