Effects of an American Heart Association Step I Diet and Weight Loss on Lipoprotein Lipid Levels in Obese Men With Silent Myocardial Ischemia and Reduced High-Density Lipoprotein Cholesterol

Leslie I. Katzel, Patricia J. Coon, Jana Dengel, and Andrew P. Goldberg

Reduced plasma concentrations of high-density lipoprotein cholesterol (HDL-C) are a risk factor for coronary artery disease (CAD). In this study, we examined the sequential effects of an isocaloric American Heart Association (AHA) step I diet and a hypocaloric AHA step I diet (AHA step I diet + weight loss) on lipoprotein lipid levels in 14 middle-aged and older (60 ± 6 years, mean ± SD) obese (body mass index [BMI] > 27 kg/m^2) nondiabetic men with exercise-induced silent myocardial ischemia (SI) and reduced HDL-C levels (0.85 ± 0.14 mmol/L). Nine men of comparable age and obesity and with no evidence of exercise-induced ischemia that were evaluated longitudinally served as metabolic controls. In men with SI, after 3 months on the isocaloric AHA step I diet plasma triglyceride (TG) levels decreased by 26% (2.25 ± 0.66 to 1.67 ± 0.69 mmol/L, $P < .005$), cholesterol by 12% (5.24 ± 0.84 to 4.62 ± 0.78 mmol/L, $P < .01$), and low-density lipoprotein cholesterol (LDL-C) by 10% (3.40 ± 0.69 to 3.05 ± 0.70 mmol/L, $P < .01$). However, plasma HDL-C levels also decreased by 7% (0.85 ± 0.14 to 0.79 ± 0.13 mmol/L, $P < .05$). Subsequent weight loss (11 ± 4 kg) in conjunction with the AHA step I diet resulted in an additional decrease of 24% in TG ($P < .005$), 10% in cholesterol ($P < .05$), and 10% in LDL-C ($P < .05$). Plasma HDL-C levels increased by 8% ($P < .01$), thereby correcting the decline seen on the AHA step I diet alone. Postheparin hepatic lipase (HL) activity decreased with weight loss ($P < .005$), with no significant change in lipoprotein lipase (LPL) activity. There were no significant changes in lipoprotein lipids or postheparin lipolytic activity in the metabolic controls. Therefore, in men with SI, the sequential interventions of an isocaloric AHA step I diet and an AHA step I diet with weight loss decreased plasma TG levels by 44% ($P < .0001$), LDL-C levels by 18% ($P < .0001$), and the LDL-C to HDL-C ratio by 19% ($P < .005$), with no significant change in HDL-C levels. Additional treatment modalities that include supervised exercise programs and drug therapy may be warranted in older obese subjects whose HDL-C levels do not normalize with diet and weight-loss interventions alone.

REDUCED PLASMA concentrations of high-density lipoprotein cholesterol (HDL-C) are a major risk factor for coronary artery disease (CAD).[1,2] Major causes of reduced levels of HDL-C include obesity, physical deconditioning, glucose intolerance/hyperinsulinemia, cigarette smoking, male gender, and genetic dyslipidemias.[3] In the revised National Cholesterol Education Program (NCEP) Adult Treatment Panel II report,[4] hygienic therapies such as exercise training, smoking cessation, and weight loss are recommended as the first line of treatment for low HDL-C in the primary prevention of CAD.

Plasma levels of HDL-C and its HDL_2-C subspecies are regulated in part by the enzymes lipoprotein lipase (LPL) and hepatic lipase (HL). LPL is the rate-limiting enzyme in the clearance of triglyceride (TG)-rich lipoproteins from plasma and is involved in the formation of HDL_2-C, whereas HL plays a role in the catabolism of HDL_2-C.[5-9] Abdominal obesity and physical deconditioning are associated with reduced LPL activity and increased HL activity.[6-8,10] Therefore, abnormalities in the activities of LPL and HL may account in part for the increased TG and reduced HDL-C and HDL_2-C subspecies levels present in people with abdominal obesity.

Before participation in an intensive weight-loss and exercise program,[10,11] exercise treadmill tests were performed on healthy obese middle-aged and older men to screen for asymptomatic cardiovascular disease. Fourteen percent of the men had asymptomatic exercise-induced ST-segment depression on an exercise ECG and myocardial-perfusion abnormalities on exercise thallium scanning consistent with silent myocardial ischemia (SI), an asymptomatic manifestation of CAD. As a group, these men with SI had abdominal obesity, mildly elevated TG levels, low HDL-C levels, and elevated postheparin HL activity.[10] In accordance with the guidelines of the NCEP, this study was designed to determine the sequential effects of a low-fat, low-cholesterol American Heart Association (AHA) step I diet[12] and weight loss on lipoprotein lipid levels in men with SI.

SUBJECTS AND METHODS

Subjects

As previously reported,[10] 228 healthy obese (body mass index [BMI] > 27 kg/m^2) male volunteers aged 46 to 76 years with no prior history of CAD, diabetes, or hypertension were recruited from the Baltimore-Washington area for participation in the Fitness After Forty-five research program.[10,12] This program is a prospective intervention study that examines the effects of weight loss and aerobic exercise training on cardiovascular and metabolic function in healthy middle-aged and older men. After a history and physical examination were obtained, blood chemistry analysis was

From the Department of Medicine, Division of Gerontology, University of Maryland School of Medicine; and the Geriatric Research Education and Clinical Center, Baltimore Veterans Affairs Medical Center, Baltimore, MD.

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Address reprint requests to Leslie I. Katzel, MD, PhD, Baltimore VA Medical Center, Geriatrics Service (18), 10 N Greene St, Baltimore, MD 21201.

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performed to screen for hyperlipidemia and diabetes mellitus. Thirty-eight men were excluded based on the examination or laboratory findings: 16 with diabetes mellitus (fasting plasma glucose level >140 mg/dL[13]), 18 with hyperlipidemia defined as a plasma TG level greater than the 95th percentile Lipids Research Clinic (LRC) (290 mg/dL) or a cholesterol level greater than the 90th percentile LRC (260 mg/dL),[14] two with anemia, one with cancer, and one with renal disease. An additional 19 men dropped out because of time constraints imposed by the research, which left 170 men for further testing.

A graded exercise treadmill test to greater than 85% of the predicted age-adjusted maximal heart rate (220 minus age) was performed in these 170 men according to the protocol reported by Bruce and Horsten[15] to screen for evidence of CAD. Forty-four men (26%) had ≥1-mm asymptomatic horizontal or down-sloping ST-segment depression for 0.08 seconds after the J-point (Minnesota Code criteria[16]) on at least two occasions, consistent with exercise-induced ischemia. The 44 subjects with ischemic treadmill tests were referred for exercise thallium scintigraphy. Of 40 men who agreed to this procedure, 23 (57%) had ischemic abnormalities on exercise ECG and reversible perfusion abnormalities on thallium scans, consistent with exercise-induced SI.[17] The 23 men with SI were excluded from the Fitness After Forty-five program. Eighteen men with SI were enrolled onto a separate nutritional-intervention program, and the other five men with SI either declined to participate or were excluded by study cardiologists. They were referred to their personal physicians for further management and care. In this study, we report data on the 14 men with SI (mean age, 60 ± 6 years) that successfully completed the interventions and on nine men from the Fitness After Forty-five program of comparable age (61 ± 7 years) and obesity with normal exercise tests that were randomized to a nonintervention control group, ie, metabolic controls. The nine metabolic controls were evaluated longitudinally for 1 year. All subjects provided informed consent according to guidelines of the Francis Scott Key Medical Center and University of Maryland School of Medicine human studies institutional review boards.

Study Design

To determine the effects of a change in dietary composition on lipoprotein lipid concentrations independently from those due to weight loss, a sequential design was used. During the first intervention, men with SI were placed on an isocaloric AHA step I diet (AHA step I diet 3 months). Men with SI attended weekly sessions in which they were instructed by registered dietitians on the principles of an AHA step I diet.[12] They were told not to lose weight or change their level of physical activity. Adherence was monitored by dietary recall and analysis of 7-day food records[18] (Table 1). After 3 months on the AHA step I diet, the men were retested. To ensure dietary stability, subjects were provided weight-maintaining AHA step I diets of a composition comparable to that of their own AHA step I diets as determined by food records from the General Clinical Research Center metabolic kitchen for 6 days of metabolic testing. All subjects were weight-stable ±0.5 kg for 6 days during metabolic testing.

For the second intervention, men with SI were placed on a hypocaloric AHA step I diet (AHA step I diet + weight loss). On average, subjects were instructed to consume 300 to 500 fewer kcal/d during the weight-loss intervention than they consumed on the isocaloric AHA step I diet, which resulted in a gradual weight loss of 0.5 kg/wk. The goal was for the men to decrease their body weight by greater than 10% over a 9-month period while maintaining the diet composition of the AHA step I diet. Men attended weekly sessions that emphasized the use of behavioral techniques to reduce caloric intake. Group dynamics were developed to support and reinforce successful weight loss. Upon reaching their target weight, men with SI were then stabilized at this weight for 1 month before repeat metabolic testing. As noted previously, food records were reviewed to ensure compliance with the AHA step I diet (Table 1). At the time of metabolic retesting, men with SI were provided weight-maintaining AHA step I diets for 6 days from the General Clinical Research Center that were of comparable composition to their own AHA step I diets. Metabolic controls were studied at baseline and after 1 year of follow-up evaluation.

Table 1. Dietary Composition at Baseline and After Intervention in Men With SI (n = 14)

		AHA Step I Diet	
	Baseline	3 Months	+Weight Loss
kcal	2,590 ± 810[a]	2,230 ± 340[b]	2,020 ± 360[b]
Carbohydrate (%)	47 ± 10[a]	53 ± 7[b]	54 ± 6[b]
Protein (%)	16 ± 3[a]	18 ± 3[b]	18 ± 3[b]
Fat (%)	36 ± 8[a]	28 ± 5[b]	29 ± 6[b]
P/S	0.62 ± 0.17[a]	0.89 ± 0.28[b]	0.97 ± 0.25[b]
Alcohol (%)	3 ± 4[a]	2 ± 5[a]	1 ± 2[b]
Fiber (g/d)	19 ± 1[a]	26 ± 8[b]	26 ± 8[b]
Cholesterol (mg/d)	330 ± 130[a]	220 ± 70[b]	190 ± 70[b]

NOTE. Seven-day food records were analyzed using Nutritionist III.[18] Data are the mean ± SD. Row values with different superscripts are significantly different at $P < .05$ by repeated-measures ANOVA.

Body Composition

BMI was calculated as body weight in kilograms divided by the square of height in meters. Hydrostatic weighing to determine body density and residual lung volume measurement by helium dilution were performed before and after weight loss in men with SI and at baseline and after 1 year of longitudinal follow-up study in metabolic controls. Percent body fat was calculated using the Siri equation.[19] Regional distribution of body fat was measured as the waist to hip ratio (WHR), determined as the ratio of the minimal abdominal circumference divided by the circumference at the maximal gluteal protuberance.

Metabolic Testing

Blood samples for determination of fasting lipoprotein lipid levels were drawn into chilled EDTA (1 mg/mL blood) tubes after a 12- to 14-hour overnight fast. Plasma TG and cholesterol levels were measured enzymatically on an Abbott ABA 200 series bichromatic analyzer (Abbott, North Chicago, IL).[20,21] Since none of the subjects had a plasma TG greater than 400 mg/dL, HDL-C level was measured in a supernatant after precipitation of apolipoprotein (apo) B–containing lipoproteins with dextran sulfate.[22] Low-density lipoprotein cholesterol (LDL-C) level was calculated using the Friedewald equation.[23] Reported lipoprotein lipid values at baseline are from a single plasma sample collected while men with SI were consuming their own ad libitum diets, whereas those after the AHA step I diet and AHA step I diet with weight-loss interventions are the means from plasma samples drawn on days 4 and 6 of the weight-maintaining metabolic diet. Based on internal-standard cholesterol pool samples, there was no laboratory drift in either plasma TG, cholesterol, or HDL-C during the study period. Coefficients of variation in 63 separate assays of internal-standard control samples for plasma TG, cholesterol, and HDL-C were 3.1%, 2.8%, and 3.8%, respectively.

After lipid samples were drawn on day 6, a standardized dose of 2,280 U/m^2 body surface area beef intestinal mucosa heparin (Organon Teknika, Rockville, MD) was injected into 12 of 14 men with SI. Heparin was not administered to two men who had a

history of peptic ulcer disease. Similarly, heparin was injected into all nine metabolic controls at baseline and after 1 year of longitudinal follow-up study for measurement of postheparin lipolytic activity. Postheparin blood samples were drawn at 10 minutes into iced, EDTA-containing tubes. The blood was centrifuged immediately at 4°C, and triplicate aliquots of postheparin plasma were stored at −70°C until completion of the study, when all samples from a given subject were analyzed in the same assay. Activities of LPL and HL in postheparin plasma were measured as previously described[10] using the method reported by Krauss et al[24] with modifications as reported by Huttunen et al.[25] The interassay coefficient of variation for this assay was 10% for LPL and 7% for HL. Postheparin HL and LPL activities are expressed as micromoles free fatty acids (FFA) hydrolyzed per milliliter per hour.

Statistical Methods

Data were entered into a database designed on a VAX 3100 computer work station (Digital Equipment, Maynard, MA) for this study and transferred to a SAS data set for analysis.[26] Data distributions were checked for skewness and kurtosis. Because plasma TG was not normally distributed, it was normalized to $\log_{10}$ TG before performance of parametric analyses. Repeated-measures ANOVA was used to analyze sequential effects of the two interventions. Paired Student's *t* tests were used to compare values after a given intervention with those of the variable before such intervention, as well as variables at baseline and after completion of the two sequential interventions. All results are expressed as the mean ± SD.

RESULTS

Baseline

Baseline physical characteristics of men with SI and metabolic controls are listed in Table 2. The mean WHR of 0.99 ± 0.08 in men with SI is consistent with an upper-body or abdominal distribution of fat. Baseline fasting lipoprotein lipid concentrations measured while men with SI were consuming their own ad libitum diets were notable for mildly elevated plasma TG levels (2.25 ± 0.66 mmol/L), low HDL-C levels (0.85 ± 0.14 mmol/L), and elevated LDL-C to HDL-C ratios (4.1 ± 0.9). None of the men with SI had HDL-C levels greater than 1.05 mmol/L, and 10 of 14 had HDL-C levels less than 0.9 mmol/L (35 mg/dL), the NCEP criteria for low HDL-C levels in men.[4]

Table 2. Physical Characteristics of Study Subjects

		AHA Step I Diet	
	Baseline	3 Months	+Weight Loss
Men with SI (n = 14)*			
BMI (kg/m²)	30 ± 3[a]	30 ± 3[a]	27 ± 3[b]
Weight (kg)	96 ± 12[a]	95 ± 13[a]	85 ± 12[b]
Fat (%)	—	30 ± 4[a]	25 ± 4[b]
WHR	0.99 ± 0.08[a]	0.99 ± 0.08[a]	0.95 ± 0.07[b]
		1-Year Follow-up Study	
Metabolic controls (n = 9)†			
BMI (kg/m²)	30 ± 2	30 ± 2	
Weight (kg)	91 ± 8	91 ± 9	
Fat (%)	30 ± 4	31 ± 4	
WHR	0.97 ± 0.04	0.99 ± 0.04	

NOTE. Data are the mean ± SD.

*Row values with different superscripts are significantly different at $P < .05$ by repeated-measures ANOVA.

†There were no significance differences between values at baseline and 1-year follow-up study.

Table 3. Lipoprotein Lipid Concentrations of Study Subjects

		AHA Step I Diet	
	Baseline	3 Months	+Weight Loss
Men with SI (n = 14)*			
TG	2.25 ± 0.66[a]	1.67 ± 0.69[b]	1.27 ± 0.46[c]
Cholesterol	5.24 ± 0.84[a]	4.62 ± 0.78[b]	4.17 ± 0.75[c]
LDL-C	3.40 ± 0.69[a]	3.05 ± 0.70[b]	2.73 ± 0.61[c]
HDL-C	0.85 ± 0.14[a]	0.79 ± 0.13[b]	0.85 ± 0.15[a]
LDL-C/HDL-C	4.1 ± 0.9[a]	4.0 ± 1.3[a]	3.3 ± 0.9[b]
		1-Year Follow-up Study	
Metabolic controls (n = 9)†			
TG	1.33 ± 0.67	1.37 ± 0.52	
Cholesterol	4.43 ± 1.05	4.74 ± 1.02	
LDL-C	2.94 ± 0.78	3.23 ± 0.80	
HDL-C	0.87 ± 0.15	0.89 ± 0.15	
LDL-C/HDL-C	3.4 ± 0.5	3.6 ± 0.7	

NOTE. Data are the mean ± SD. Lipid concentrations are in mmol/L.

*Row values with different superscripts are significantly different at $P < .05$ by repeated-measures ANOVA.

†There were no significance differences between values at baseline and 1-year follow-up study.

AHA Step I Diet 3 Months

As compared with their baseline ad libitum diets, men with SI were consuming diets higher in complex carbohydrate, protein, and fiber and lower in saturated fat and cholesterol (Table 1). Based on the food record data, there was a significant decrease in calories on the AHA step I diet ($P < .05$) despite the instruction not to reduce caloric intake; nevertheless, men did not lose weight during this phase, so the weight-stable phase of the design was achieved. After 3 months on the AHA step I diet, plasma cholesterol concentrations decreased by 12% ($P < .01$) and LDL-C concentrations decreased by 10% ($P < .01$) (Table 3). Plasma TG levels declined in 13 of 14 men, which led to a 26% decrease in plasma TG levels ($P < .005$). However, plasma HDL-C levels decreased by 7% (0.85 ± 0.14 to 0.79 ± 0.13, or 30 ± 5 mg/dL, $P < .05$). As a result of the concurrent decrease in both HDL-C and LDL-C, there was no significant change in the LDL-C to HDL-C ratio (4.1 ± 0.9 to 4.0 ± 1.3, P = NS).

AHA Step I Diet With Weight Loss

After 9 months on the hypocaloric AHA step I diet, men with SI lost an average of 11 ± 4 kg (range, 7 to 14), which resulted in highly significant ($P < .0001$) decreases in BMI and percent body fat (Table 2). Of particular interest, WHR decreased from 0.99 ± 0.08 to 0.95 ± 0.07 ($P < .0001$). Based on analysis of 7-day food records, there was no significant change in dietary composition or daily caloric intake between the weight-stable intervention and the weight-loss intervention (Table 1). The AHA step I diet

with a weight-reduction intervention led to an additional 24% decrease in plasma TG ($P < .005$), 10% decrease in total cholesterol ($P < .05$), and 11% decrease in LDL-C ($P < .05$) (Table 3). Importantly, HDL-C increased by 8% (0.79 ± 0.13 to 0.85 ± 0.15, or 33 ± 6 mg/dL, $P < .01$) on the hypocaloric diet, which thereby negated the decrease in HDL-C observed with the isocaloric AHA step I diet intervention. Furthermore, there was a 17% decrease in the LDL-C to HDL-C ratio ($P < .01$). The increment in HDL-C levels with weight loss correlated inversely with the decrement in BMI ($r = .62$, $P < .05$). Therefore, in men with SI, the sequential interventions of AHA step I diet and AHA step I diet with weight loss decreased plasma TG levels by 44% ($P < .0001$; Fig 1A), total cholesterol levels by 21% ($P < .0001$), LDL-C levels by 18% ($P < .0001$; Fig 1B), and the LDL-C to HDL-C ratio by 19% ($P < .005$), with no significant change in HDL-C levels (Fig 1C). By contrast, there were no significant changes in body composition or lipoprotein lipid concentrations in metabolic controls at the 1-year follow-up evaluation. Thus, in men with SI, changes in plasma levels of TG, total cholesterol, and LDL-C and the LDL-C to HDL-C ratio in response to the sequential interventions of the isocaloric AHA step I diet and the AHA step I diet + weight loss differed significantly ($P < .001$) from response seen in longitudinal follow-up study of metabolic controls.

Postheparin HL and LPL Activities

To determine whether changes in lipoprotein lipid levels after weight loss in men with SI were related to changes in activities of LPL and HL, activities of these enzymes were measured in postheparin plasma. With weight loss, postheparin HL activity decreased in each subject with SI (Fig 2A). The mean HL activity decreased by 22% ($P < .0001$; Table 4), whereas there was no significant change in LPL activity with weight loss (Fig 2B, Table 4). By comparison, there were no significant changes in HL or LPL activities in metabolic controls at the 1-year follow-up study (Table 4). In men with SI, the change in postheparin HL activity in response to the sequential interventions differed significantly ($P < .001$) from responses seen in longitudinal follow-up study of metabolic controls. The decrease in postheparin HL activity with weight loss correlated with the change in BMI ($r = .72$, $P < .05$). There was no significant correlation between the change in HDL-C levels with weight loss and the change in postheparin HL activity ($r = -.15$, P = NS) or LPL activity ($r = .22$, P = NS) in men with SI.

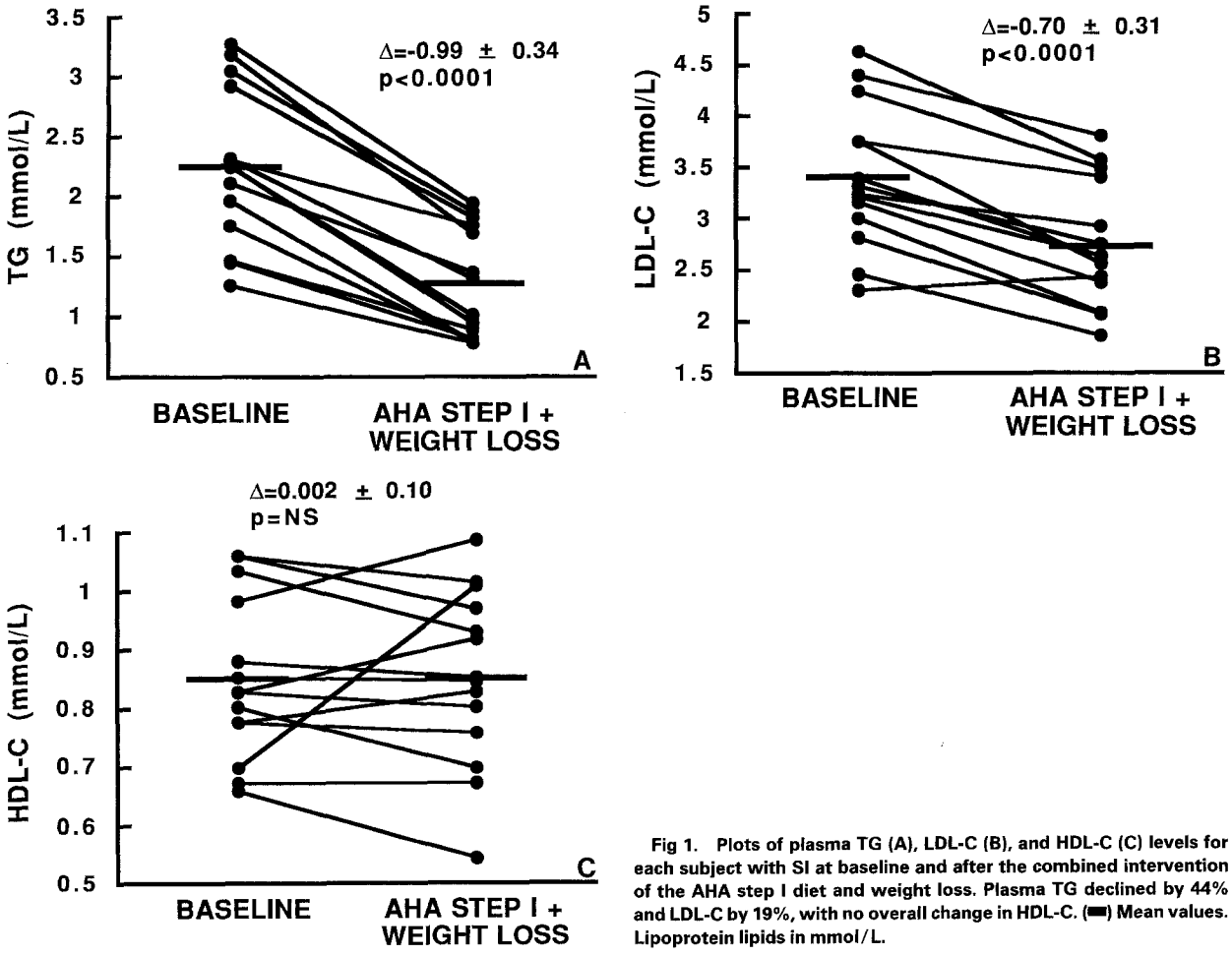

Fig 1. Plots of plasma TG (A), LDL-C (B), and HDL-C (C) levels for each subject with SI at baseline and after the combined intervention of the AHA step I diet and weight loss. Plasma TG declined by 44% and LDL-C by 19%, with no overall change in HDL-C. (▬) Mean values. Lipoprotein lipids in mmol/L.

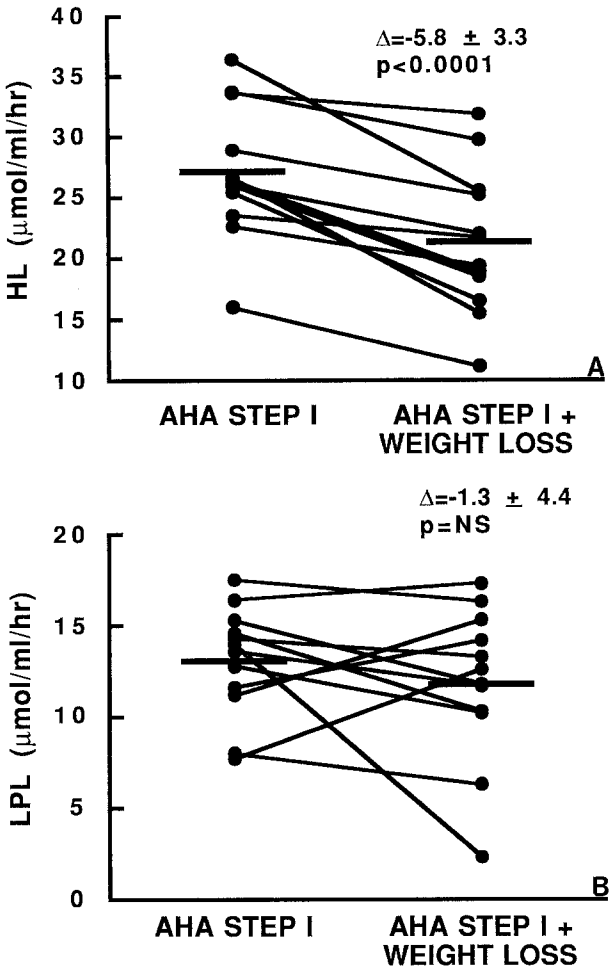

Fig 2. Plots of postheparin HL (A) and LPL (B) activity for each subject with SI on the AHA step I diet and after the combined intervention of the AHA step I diet and weight loss. Postheparin HL activity decreased in response to weight loss in each man with SI ($P < .0001$), with no significant change in postheparin LPL activity. (▬) Mean values. Postheparin lipolytic activity expressed in μmol fatty acids hydrolyzed/mL/h.

Table 4. Postheparin Lipase Activities in Study Subjects

	AHA Step I Diet	
	3 Months	+Weight Loss
Men with SI (n = 12)†		
LPL	13 ± 3	12 ± 4
HL	27 ± 6	21 ± 6*
	Baseline	1-Year Follow-Up Study
Metabolic controls (n = 9)†		
LPL	13 ± 6	14 ± 5
HL	22 ± 3	25 ± 9

NOTE. Data are the mean ± SD. Activities in μmol FFA hydrolyzed/mL/h.

*$P < .0001$ compared with AHA step I diet by paired t-test.

†There were no significance differences between values at baseline and 1-year follow-up study.

DISCUSSION

This study was designed to investigate changes in plasma levels of lipoprotein lipids in response to the AHA step I diet and weight loss in obese middle-aged and older men with SI, a manifestation of CAD. This treatment approach is in agreement with the revised guidelines of the NCEP, which emphasize the role of nonpharmacologic therapy in the treatment of dyslipoproteinemia.[4] In these obese sedentary older men with low HDL-C levels and SI, the isocaloric AHA step I diet decreased plasma concentrations of LDL-C. This change is clearly beneficial in reducing the risk for CAD, but was accompanied by a potentially detrimental reduction in plasma concentration of HDL-C. By contrast, the combination of weight loss and the AHA step I diet was more effective in decreasing TG and LDL-C levels than the isocaloric AHA step I diet alone, but without the adverse effect on HDL-C levels. Although there was no significant change in HDL-C levels with intervention, there was a 19% decrease in the LDL-C to HDL-C ratio due to a reduction in LDL-C levels. Therefore, weight reduction is an important component of the dietary therapy for dyslipidemia in obese older individuals. Weight reduction will also have beneficial effects on the glucose intolerance/insulin resistance and hypertension that often coexist in older individuals with abdominal obesity.

Low-fat, high-carbohydrate diets often increase plasma TG concentrations,[27] particularly when there is a sudden increase in dietary carbohydrate content.[28] The carbohydrate-induced increase in plasma TG levels is often transient.[28,29] In our study, we avoided the potentially confounding effects of abrupt changes in dietary composition on lipoprotein lipid levels. After 3 months on the AHA step I diet, plasma TG levels decreased in 13 of 14 men with SI. Furthermore, plasma TG levels decreased in all 14 men with SI after completion of the AHA step I diet with weight-loss intervention. Therefore, in these nondiabetic obese older men, weight loss in combination with the AHA step I diet significantly decreased plasma TG levels.

Plasma HDL-C concentrations decreased on the AHA step I diet. Subjects in this study made multiple changes in the composition of their diets, which included consumption of less total fat, less saturated fat, less cholesterol, more carbohydrates, and more dietary fiber. Each of these changes in dietary composition may independently affect plasma HDL-C levels, since reductions in HDL-C levels have been noted in individuals who consume diets high in complex carbohydrates, low in total dietary fat, or high in the absolute amount of polyunsaturated fatty acids.[28,30-32] In contrast, dietary monounsaturated fatty acids do not appear to decrease HDL-C levels when substituted for saturated fatty acids.[33,34] Kinetic studies indicate that in a given individual, diet-induced changes in HDL-C levels may result from changes in the production rate of the major HDL apolipoprotein, apo A-I, whereas differences in HDL-C levels between people on a given diet may result from differences in apo A-I fractional catabolic rates.[35] Given the complexity of metabolic regulation of HDL-C levels, the change in HDL-C levels in response to dietary intervention is probably multifactorial in nature.

There is no consensus on whether diet-induced reductions in HDL-C levels are harmful. Indeed, epidemiologic data demonstrate that populations that consume low-fat diets have low HDL-C levels, low LDL-C levels, and a reduced prevalence of CAD,[36] which suggests that, provided the LDL-C level is also low, a diet-induced decrease of HDL-C level does not increase CAD risk. These analyses must also take into consideration the effects of low-fat diets on the circulating levels and composition of LDL-C, intermediate-density lipoproteins, and very–low-density lipoproteins, since a reduction in the atherogenic particles may balance the adverse effects of diet-induced reductions in HDL-C. In addition, since plasma HDL-C is composed of a heterogenous mixture of particles, measurement of total HDL-C content alone may not adequately quantify the effects of diet and weight loss on the cardioprotective HDL-C subspecies. In a study reported by Puchois et al,[37] as compared with controls without CAD, patients with CAD had marked reductions in HDL-C particles that contained only apo A-I, with no difference in levels of HDL-C particles that contained both apo A-I and A-II. This suggests that apo A-I–containing particles are the major cardioprotective species of HDL-C. Therefore, if low-fat diets preferentially affect one class of particles more than the other, ie, a decrease of particles that contain both apo A-I and apo A-II with a preservation or even an increase in the apo A-I–only particles, one could account for these epidemiologic findings.

A number of studies have examined the effect of weight loss on lipoprotein lipid levels. In a study reported by Wolf and Grundy,[38] HDL-C increased by 32% in response to an average weight loss of 21 kg. Wood et al[39] compared the effects of a weight-reducing hypocaloric AHA step I diet alone or in combination with exercise in obese men and women. In that study, plasma HDL-C levels increased by 13% in men who exercised and dieted, as compared with 2% in those men who only dieted. In women, HDL-C levels remained the same in women who exercised and dieted, whereas they decreased by 10% in those who only dieted. In another study reported by Wood et al[40] of the effects of weight loss on lipoprotein lipids in obese men, a mean weight loss of 8 kg was associated with an 11% increase in HDL-C and a 17% decrease in TG, with no significant change in LDL-C. Although the overall results in our study were similar to those reported by Wood et al, it should be noted that our subjects were older and more obese and had higher TG and lower HDL-C levels than men in their study. Additionally, we measured postheparin HL and LPL activities at baseline and after weight-loss intervention, thus providing insight into possible mechanisms that regulate the change in lipoprotein lipid levels with weight loss. Therefore, the two studies are complementary.

Previous investigations have demonstrated an inverse association between HL activity and HDL-C levels.[6-10,41-44] Indeed, we previously reported that men with SI enrolled in the current study had significantly higher postheparin HL activity and lower HDL-C levels than age- and obesity-matched controls with normal exercise tests.[10] There was a significant decrease in postheparin HL activity with weight loss, with no significant change in postheparin LPL activity. These results are consistent with cross-sectional studies[6,9,10] that demonstrate a relationship between postheparin HL activity and obesity and with intervention studies that demonstrate significant decreases in postheparin HL activity in individuals who lose weight either through hypocaloric dieting or after exercise training.[42-44] Although in our study there was no significant relationship between the change in HDL-C and either LPL or HL activities with weight loss, others have reported significant relationships between the change in postheparin HL and LPL activities and the change in HDL-C, HDL_2-C, and HDL_2-C mass.[42,44] Since the activity of HL decreased in all subjects who lost weight, this association seems related despite the lack of a statistically significant correlation coefficient. Given the purported role of HL in the catabolism of HDL_2-C,[6-9] this suggests that the increase in HDL-C with weight loss may be mediated in part through reduced catabolism of HDL-C by HL.

In summary, our results demonstrate that in obese sedentary older men with asymptomatic exercise-induced ischemia, weight reduction in conjunction with the AHA step I diet decreases plasma concentrations of TG and LDL-C but does not significantly increase HDL-C levels. However, the combination of the AHA step I diet and weight loss failed to increase HDL-C levels to more than 35 mg/dL in 10 of 14 men. This may be due in part to the fact that even after moderate weight loss, some of the men were still significantly heavier than their ideal body weight and also maintained an upper-body distribution of fat, whereas others may have genetic dyslipidemias that contribute to their low HDL-C levels. Given the increased risk of myocardial infarction and sudden cardiac death in older men with SI,[45] particularly in those with low HDL-C,[46] additional treatment modalities that include supervised exercise programs and drug therapy may be warranted in subjects whose LDL-C and HDL-C levels do not normalize with diet and weight-loss interventions alone.

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