Consumption of a Defined, Plant-Based Diet Reduces Lipoprotein(a), Inflammation, and Other Atherogenic Lipoproteins and Particles Within Four Weeks

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SUMMARY

Background: Lipoprotein(a) [Lp(a)] is a highly atherogenic lipoprotein and is minimally effected by lifestyle changes. While some drugs can reduce Lp(a), diet has not consistently shown definitive reduction of this biomarker. The effect of consuming a plant-based diet on serum Lp(a) concentrations have not been previously evaluated.

Hypothesis: Consumption of a defined, plant-based for four weeks reduces Lp(a).

Methods: Secondary analysis of a previous trial was conducted, in which overweight and obese individuals (n=31) with low-density lipoprotein cholesterol concentrations >100 mg/dL consumed a defined, plant-based diet for four weeks. Baseline and 4-week labs were collected. Data were analyzed using a paired samples t-test.

Results: Significant reductions were observed for serum Lp(a) (-32.0 ± 52.3 nmol/L, P = 0.003), apolipoprotein B (-13.2 ± 18.3 mg/dL, P <0.0005), low-density lipoprotein (LDL) particles (-304.8 ± 363.0 nmol/L, P <0.0005) and small-dense LDL cholesterol (-10.0 ± 9.2 mg/dL, P <0.0005). Additionally, serum interleukin-6 (IL-6), total white blood cells, lipoprotein-associated phospholipase A2 (Lp-PLA2), high-sensitivity c-reactive protein (*hs*-CRP) and fibrinogen were significantly reduced (P ≤ 0.004).

Conclusions: A defined, plant-based diet has a favorable impact on Lp(a), inflammatory indicators, and other atherogenic lipoproteins and particles. Lp(a) concentration was previously thought to be only minimally altered by dietary interventions. In this protocol however, a defined plant-based diet was shown to substantially reduce this biomarker. Further investigation is required to elucidate the

specific mechanisms that contribute to the reductions in Lp(a) concentrations, which may include alterations in gene expression.

Keywords: Lipoproteins, general clinical cardiology/adult, preventive cardiology, vegetarian diet

INTRODUCTION

Lipoprotein(a) [Lp(a)] is an atherogenic lipoprotein structurally similar to low-density lipoprotein cholesterol (LDL-C), although synthesis occurs through independent pathways. Key differences include the linkage of apolipoprotein B100 (Apo-B) to apolipoprotein(a) on the LDL surface.[1,2] It has been estimated that expression of the genomic region encoding apolipoprotein(a) (*LPA* gene) accounts for ~90% of plasma Lp(a) concentrations.[3] Elevated Lp(a) is independently associated with cardiovascular disease[4], and the LPA gene was observed to have the strongest genetic link to cardiovascular disease[5]. Individuals with Lp(a) plasma concentrations >20 mg/dL have twice the risk of developing cardiovascular disease and approximately 25% of the population may have this plasma concentration[6]. The mode of action by which Lp(a) exerts its atherogenic effect is likely similar to that of LDL-C, by deposition in the sub-endothelial space and uptake by macrophages mediated via the VLDL receptor.[7] Lp(a) is particularly atherogenic due to its unique property of being a carrier of oxidized phospholipids, in addition to its higher binding affinity to negatively charged endothelial proteoglycans.[8] Lp(a) can facilitate endothelial dysfunction when concentrations are elevated likely due to this effect.[9]

While PCSK9 inhibitors, high dose atorvastatin, ezetimibe and niacin have resulted in significant reductions in Lp(a) [10-12], lifestyle interventions have not reliably demonstrated reduced Lp(a) to a clinically significant degree. Interestingly, even high saturated fat and high cholesterol diets known to induce hypercholesterolemia have had little influence on plasma Lp(a) concentrations.[13] Despite the lack of evidence in the literature indicating a relationship between diet and Lp(a) concentrations, a defined,

plant-based has not been previously evaluated with respect to its potential effect to reduce Lp(a). Previous investigations have found that a very-high fiber diet comprised of vegetables, fruits and nuts can reduce LDL-C by 33% and Apo-B by 26%[14], although Lp(a) was not measured. Since such a diet can result in dramatic reductions in LDL-C and Apo B, secondary analysis of a previously published investigation[15] employing a similar plant-based diet were analyzed to evaluate if Lp(a) could be significantly reduced after four weeks among other inflammatory indicators and atherogenic lipoproteins and particles.

METHODS

Study Population

Participants were subjects of a previous study in which written informed consent was obtained to draw blood for analysis.[15] Laboratory reports for each subject included biomarkers used for clinical purposes, and selected biomarkers are included in the present investigation. The study protocol was approved by the Texas Woman's University Institutional Review Board - Houston.

The study protocol has been previously described.[15] Briefly, all participants were registered new patients of a cardiovascular center and were hypertensive (systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg), had elevated LDL-C (≥100 mg/dL) and excess body weight (body mass index ≥25 kg/m^2) at baseline. Exclusionary criteria included current tobacco use, current drug abuse, excessive alcohol use (>2 glasses of wine or equivalent for men or >1 glass of wine or equivalent for woman), a current cancer diagnosis, an ongoing clinically defined infection, a mental

disability that would prevent a participant from following the study protocol, an estimated glomerular filtration rate <60 mg/dL, current pregnancy or lactation, a hospitalization within the past 6 months, and previous exposure to the nutrition program.

Intervention

Participants were instructed to consume a defined, plant-based diet for four weeks *ad-libitum* which included the consumption of foods within a food classification system[15]. These foods fell within food levels 0-4b of the food classification system (Supplementary table1). Briefly, excluded were animal products, cooked foods, free oils, soda, alcohol, and coffee. Allowed for consumption were raw fruits, vegetables, seeds and avocado. Small amounts of raw buckwheat and oats were also permitted. Vitamin, herbal, and mineral supplements were to be discontinued unless otherwise clinically indicated. All meals and snacks were provided to subjects, although they were free to consume food on their own within food levels 0-4b. In addition, subjects were not advised to alter their exercise habits. Adherence was measured daily as previously described[15] with an adherence assessment tool. Participants indicated in writing each day whether they were adherent. Dietary recalls (24-hour) were conducted by a trained nutritionist at baseline and at four weeks. Nutrient intake was analyzed by the Nutrition Data System for Research software (University of Minnesota, version 2016). No lipid lowering medications were altered throughout the intervention.

Measures

After a 12-hour fast, the following plasma biomarkers were obtained at baseline and after 4-weeks: total cholesterol (Total-C), LDL-C, high-density lipoprotein

cholesterol (HDL-C), triglycerides, LDL particles (LDL-P), small-dense low-density lipoprotein cholesterol (sdLDL-C), Apo-B, high-density lipoprotein 2 cholesterol (HDL2-C), apolipoprotein A-1 (Apo A-1) and Lp(a). Additionally, high-sensitivity c-reactive protein (*hs*-CRP), endothelin, interleukin-6 (IL-6), tumor necrosis factor alpha (TNF-a), lipoprotein-associated phospholipase A2 (Lp-PLA2), myeloperoxidase, fibrinogen, troponin-I, N-terminal pro b-type natriuretic peptide (NT-proBNP), total white blood cell count (WBC), neutrophil count, lymphocyte count, monocyte count, eosinophil count and basophil count were documented. These specific biomarkers of interest were analyzed by either True Health Diagnostics (Frisco, TX, USA) or Singulex (Alameda, CA, USA) depending on the subject's health insurance. The same company that analyzed the baseline labs for a participant was used for the follow-up labs to ensure consistency.

Data Analysis

Paired samples t-tests were used for the analysis of biochemical measures at baseline and 4-weeks, and significance was confirmed with non-parametric tests. Significance was determined to be a P-value less than 0.05. SPSS (version 24) was used for data analysis.

RESULTS

Baseline demographics are indicated in Table 1. Subjects represent a sample that was 81% obese with multiple clinical diagnoses. Two-thirds of subjects were women and 80% were African American.

Insert *Table 1—Baseline characteristics and clinical diagnoses*

Adherence to the dietary intervention was ~87% over the course of the four weeks as measured by the daily adherence assessment tool. Food group consumption is indicated in Table 2 at baseline and 4-weeks. Notably, total fruit consumption increased from 1.3 ± 2.0 servings to 11.8 ± 10.4 servings (808% increase, P <0.0005) and total vegetable consumption increased 2.7 ± 2.0 servings to 16.0 ± 9.2 servings (493% increase, P <0.0005). Additionally, total animal product consumption decreased from 7.9 ± 4.7 servings to 0.4 ± 1.4 servings (95% decrease, P = 0.001). The consumption of avocados, dark-green vegetables, deep-yellow vegetables, tomatoes and other vegetables also significantly increased (P ≤ 0.006). A decreased consumption of white potatoes, fried potatoes, total grains, refined grains, whole grains, added oils, added animal fat, red meat, white meat, eggs and dairy were also observed (P ≤ 0.027). The consumption of sweets (5% decrease, P = 0.90) and the consumption of nuts/seeds (17% increase, P = 0.736) did not significantly change between baseline and 4-weeks.

Insert Table 2—Number of food group servings at baseline and 4-weeks

Body weight, BMI, total cholesterol, LDL-C, HDL-C and triglycerides (Table 3) were significantly reduced after 4-weeks of the dietary intervention (P ≤0.008). Lp(a) was also significantly reduced (-32.0 ± 52.3 nmol/L, P = 0.003). In addition, LDL-P, sdLDL-C, Apo-B, HDL2-C and Apo A-1 were significantly reduced (P ≤0.03). Of the atherogenic lipoproteins, sdLDL-C had the greatest relative reduction of approximately

30% (Figure 1). Lp(a) reduced 16% which was proportional to the decrease in Total-C, triglycerides and LDL-P..

Insert Figure 1—Percent change of atherogenic lipoproteins and particles from baseline to 4-weeks.

Insert Table 3—Atherogenic lipoproteins and particles at baseline and 4-weeks

Of the inflammatory indicators, *hs*-CRP, IL-6, Lp-PLA2 and fibrinogen significantly decreased ($P \leq 0.004$) (Table 4). The WBC, neutrophil, lymphocyte, monocyte, eosinophil and basophil count also significantly decreased ($P \leq 0.033$). Interestingly, no statistically significant changes were observed for endothelin-1, TNF-a, myeloperoxidase, troponin-I or NT-proBNP ($P \geq 0.056$) between baseline and 4-weeks.

Insert Table 4—Inflammatory and other cardiovascular indicators at baseline and 4-weeks

DISCUSSION

The consumption of a defined, plant-based diet resulted in a significant reduction in Lp(a) after four weeks; thus, the study hypothesis was accepted. The reduction in Lp(a) was profound and is one of the largest reductions due to lifestyle reported in the literature. The magnitude of change was comparable to other leading medical therapies, such as niacin (~20% reduction) and PCSK9 inhibitors (~25% reduction).[12] It is important to note that this dietary intervention rapidly reduced Lp(a) by 16% in only four weeks, whereas shorter duration niacin and PCSK9 inhibitor drug trials typically lasted 8-12 weeks. It should also be noted that niacin may reduce inflammation, such as *hs*-

CRP, by 15% after 3 months, although PCSK9 inhibitors do not.[16, 17] After four weeks, the dietary intervention reduced *hs*-CRP by 30.7%. In addition, IL-6, Lp-PLA2, fibrinogen and white blood cells were significantly reduced, as were sdLDL-C, LDL-P and Apo B, all of which represent a systemic, cardio-protective effect.[18-24] Thus, the use of this single dietary approach in the clinical setting, versus multiple drug therapy, may be an appropriate tool in treating complex patients with a myriad of elevated CVD-related biomarkers.

Elevated Apo A1, HDL-C and HDL2-C are associated with reduced cardiovascular disease risk.[24, 25] While these HDL fractions were significantly reduced in this trial, this is a common phenomenon observed when consuming plant-based diets. A systematic review and meta-analysis of plant-based observational and clinical trials found that while HDL-C was significantly reduced compared to those consuming non-vegetarian diets, LDL-C and Total-C were also reduced.[26] Despite reductions in HDL-C, those who consumed plant-based diets had a 25% reduced incidence of ischemic CVD compared with non-vegetarian counterparts.[27]

Lp(a) concentrations in the present study represent a high-risk population.[28] This may be explained by the higher proportion of African Americans in this sample, as African Americans may have higher Lp(a) concentrations compared with Caucasians.[29] An evaluation of 532,359 patients found that an Lp(a) concentration >50 mg/dL was common among patients.[30] This range roughly corresponds to the mean nmol/L Lp(a) concentration observed in the present study.

Effect of Weight Loss on Plasma Lp(a) Concentrations

An energy restricted diet was found to independently reduce serum Lp(a) in those with baseline concentrations >20 mg/dL, but not <20 mg/dL.[31] Further studies have found that weight loss may not independently reduce Lp(a) concentrations. A pooled analysis of cohorts found that as weight loss ensued, Lp(a) concentrations surprisingly increased.[32] Baseline Lp(a) concentrations on average between the 4 cohorts analyzed were ~40 mg/dL, well above the >20 mg/dL threshold reported in the initial study.[31] Other investigations examining the effect of weight loss on Lp(a) concentration have not demonstrated a relationship between these two variables. [33, 34] Interestingly, the emphasis on consuming plant-based foods, even with a calorie restricted diet, did not result in Lp(a) reductions compared with a calorie restricted red meat centered diet.[35] The plant-centered diet in this trial[35] still contained a significant number of calories derived from animal based sources in addition to processed plant foods. Also, both diets contained similar quantities of dietary fiber, a measure of plant-food intake. Based on these weight loss trials, Lp(a) concentration is likely not influenced by weight reduction.

Effect of Diet on Plasma Lp(a) Concentrations

Other trials using diets emphasizing plant-based foods have not demonstrated similar results. A low-fat and low-saturated fat diet with an increased intake of fruits and vegetables interestingly increased Lp(a) concentrations[36]. Subjects consumed 4-5 servings of fruits or berries and 5-6 servings of vegetables daily for five weeks and all food was provided. It is important to note that subjects still consumed animal products throughout the intervention[36] which included dairy products and lean meats. The fiber content (40g versus 51g in the present study) was not as high as would be expected

when consuming a higher quantity of plant-foods, and the number of fruits and vegetables did not meet the levels observed in the present study (11.8 servings of fruits and 16 servings of vegetables). Based on this data, it is probable that exclusively increasing fruit and vegetable intake is not sufficient to elicit reduced Lp(a) concentrations.

It has also been reported that a low-carbohydrate, high-fat diet (45% carbohydrate, 40% fat) may have a favorable impact on Lp(a) concentrations compared with a high-carbohydrate, low-fat diet (65% carbohydrate, 20% fat), although it is unclear as to what precisely was consumed on either of these diets.[37] In addition, the differences were small, as only a 2.17 mg/dL difference was observed between both groups, and baseline Lp(a) concentrations were <20 mg/dL. The Omni Heart Trial also found that replacing calories from carbohydrates and protein with unsaturated fats produced a smaller increase in Lp(a) comparatively, but both diets still elicited increased plasma Lp(a) compared with baseline. The differences between groups were also small at the end of the intervention (<4 mg/dL difference).[38]

In individuals with low baseline Lp(a) concentrations (~5.5 mg/dL), the consumption of copious saturated fat, cholesterol (derived from egg consumption) and polyunsaturated fat did not influence Lp(a) concentrations.[13] Carbohydrate intake was low in this trial as well (39% to 46% carbohydrate as a percent of energy). While fat consumption does not appear to influence serum Lp(a) concentrations in the fasting state, a variety of fats may significantly increase postprandial, transient plasma Lp(a) concentrations over the course of 8 hours.[39] Investigators found that linoleic, oleic, palmitic and stearic acid all resulted in significant transient increases in Lp(a)

concentrations which closely tied to a proportional increase in triacylglycerol concentrations. While saturated fats, stearic acid and palmitic acid, appeared to have the greatest increase in serum Lp(a) compared with oleic acid and linoleic acid, this differing response did not reach statistical significance.

Mechanisms Contributing to Reduced Plasma Lp(a)

The observed reduction in Lp(a) in the present study may be due to decreased hepatic synthesis of apolipoprotein(a) and Apo B. This may be in part due to decreased expression of the LPA gene. Since the LPA gene is almost exclusively expressed in the liver[40], hepatic influences, including the production of *hs*-CRP and inflammatory cytokines, such as IL-6, may upregulate LPA gene expression.[41] Indeed, those with inflammatory conditions may have increased Lp(a) concentrations compared with healthy controls.[42]

Current data in our plant-based study supports this hypothesis, as reduced *hs*-CRP and IL-6 was observed. In contrast, previous studies utilizing plant-centered diets to reduce Lp(a) were unsuccessful, as animal products were still substantially consumed.[35, 36] Animal-based foods, including lean meat, can induce a postprandial inflammatory response, including increased *hs*-CRP and IL-6.[43] Pooled data of those consuming non-vegan, plant-based diets have shown reduced *hs*-CRP and IL-6[44], although to a lesser extent compared with the present study (*hs*-CRP; -0.55 mg/dl vs -2.42 mg/dL, IL-6; -0.25 pg/mL vs -0.64 pg/mL). The elimination of animal products and processed foods completely on a defined, plant-based diet may be a more prudent dietary strategy to avoid potential fluctuations in inflammation. Thus, the fact that there

were only minimally processed plant foods consumed during this dietary intervention may account for the observed reduction in serum Lp(a) concentrations that may be associated with reduced LPA gene expression. Further mechanistic research is needed to confirm this hypothesis.

Strengths and Limitations

The high dietary adherence and provision of all food to subjects supports the conclusion that the intervention likely fully accounted for the observed biochemical changes among the subjects. Furthermore, the study took place in an outpatient clinical setting with established patients providing a real-world example of a standard clinical practice. This study provides a model for the implementation of this intervention across other medical practices. In contrast, a limitation in the design of this study was the lack of a control group and the small sample size. A larger sample size and a control group would be needed to strengthen a causal relationship.

CONCLUSION

A defined, plant-based diet has a favorable impact on Lp(a) and other atherogenic lipoproteins and particles. Lp(a) concentration was previously thought to be only minimally altered by lifestyle interventions. In this study, however, a defined plant-based diet resulted in a substantial reduction in Lp(a) in only four weeks. Further investigations are warranted to elucidate the specific mechanisms that contribute to reduced Lp(a) concentrations, which may include alterations in LPA gene expression mediated via hepatic inflammation.

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Figure 1 Legend: Percent change of atherogenic lipoproteins and particles from baseline to 4-weeks. All variable changes indicated are significant ($P < 0.05$). List of abbreviations: Lp(a), lipoprotein(a); Total-C, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Apo-B, apolipoprotein B100; LDL-P, low-density lipoprotein particles; sdLDL-C, small-dense low-density lipoprotein cholesterol; HDL2-C, high-density lipoprotein-2 cholesterol; Apo A-1, apolipoprotein A-1.

Table 1-*Baseline characteristics and clinical diagnoses*

	Participants[1]
n	31
Age (years)	53.4 (32-69)
Sex	
Male	10 (33%)
Female	21 (67%)
Race, ethnicity	
African American	25 (80%)
Hispanic	3 (10%)
White	3 (10%)
Mean BMI (kg/m^2)	37.5 ± 8.3
Overweight (25–29.9 kg/m^2)	6 (19%)
Obesity Class 1 (30–34.9 kg/m^2)	6 (19%)
Obesity Class 2 (35–39.9 kg/m^2)	10 (33%)
Obesity Class 3 (≥40 kg/m^2)	9 (29%)
Current Diagnoses	
Coronary Artery Disease	10 (33%)
Type II Diabetes Mellitus	8 (27%)
Arthritic condition	7 (23%)
Pre-diabetes	5 (17%)

[1]Data are mean (range) unless otherwise indicated.
List of abbreviations: BMI, body mass index.

Table 2—Number of food group servings at baseline and 4-weeks[1]

Food group	Serving size	Baseline[2]	Final[2]	Change[3]	*P*[4]
Fruits, Total	1/2 cup chopped, 1/4 cup dried or 1 medium piece	1.3 ± 2.0	11.8 ± 10.4	808% (10.5 ± 10.8)	<0.0005
Avocado	1/2 cup chopped	0.1 ± 0.2	0.9 ± 0.9	800% (0.8 ± 0.9)	<0.0005
Vegetables, Total	1/2 cup chopped or 1 cup raw leafy	2.7 ± 2.0	16.0 ± 9.2	493% (13.3 ± 9.2)	<0.0005
Dark-green Vegetables	1/2 cup chopped or 1 cup raw leafy	0.7 ± 1	5.2 ± 3.8	643% (4.5 ± 4.0)	<0.0005
Deep-yellow Vegetables	1/2 cup chopped	0.2 ± 0.4	1.2 ± 1.1	500% (1.0 ± 1.3)	<0.0005
Tomatoes	1/2 cup chopped	0.4 ± 0.5	1.7 ± 2.4	325% (1.3 ± 2.4)	0.006
Other Vegetables	1/2 cup chopped	1.4 ± 1.2	7.9 ± 6.6	464% (6.5 ± 6.3)	<0.0005
White Potatoes[5]	1/2 cup chopped or 1 medium baked potato	0.3 ± 0.7	0.0 ± 0.0	-100% (-0.3 ± 0.7)	0.03
Fried Potatoes	1/2 cup chopped or 70g french fries	0.5 ± 0.9	0.1 ± 0.3	-80% (-0.4 ± 0.9)	0.027
Grains, Total	1 slice of bread or half cup cooked cereal	5.7 ± 3.5	0.7 ± 0.9	-88% (-5.0 ± 3.6)	<0.0005
Refined Grains	1 slice of bread or half cup cooked cereal	3.8 ± 2.7	0.2 ± 0.7	-95% (-3.6 ± 3.0)	<0.0005
Whole Grains	1 slice of bread or half cup cooked cereal	1.9 ± 2.6	0.5 ± 0.7	-74% (-1.4 ± 2.7)	0.007
Sweets[6]	4 g of sugar, 1 tbsp honey or 2 tbsp syrup	1.8 ± 2.3	1.7 ± 1.5	-5% (-0.1 ± 2.7)	0.90
Nuts/seeds	1/2 oz	1.2 ± 3.0	1.4 ± 1.6	17% (0.2 ± 3.4)	0.736
Added Oils	1 tsp	3.2 ± 3.5	0.1 ± 0.2	-97% (-3.1 ± 3.5)	<0.0005
Added Animal Fat	1 tsp	1.3 ± 2.3	0.0 ± 0.1	-100% (-1.3 ± 2.3)	0.005
Animal Products, Total[7]	1 oz	7.9 ± 4.7	0.4 ± 1.4	-95% (-7.5 ± 5.3)	0.001
Red Meat	1 oz	2.1 ± 2.9	0.1 ± 0.2	-95% (-2.0 ± 3.0)	<0.0005
White Meat	1 oz	3.9 ± 3.7	0.2 ± 1.1	-95% (-3.7 ± 4.1)	<0.0005
Eggs	1 large egg	0.5 ± 0.7	0.0 ± 0.1	-100% (-0.5 ± 0.7)	0.002
Dairy	1 cup of milk/yogurt or 1.5 oz of cheese	1.5 ± 1.6	0.1 ± 0.3	-93% (-1.4 ± 1.7)	<0.0005

[1] Data are for subjects who completed 24-hour recalls at both baseline and 4-weeks (n=30).

[2] Data are listed in serving size and are presented as mean ± standard deviation.

[3] Data indicated as % change (mean ± standard deviation)

[4] Paired samples t-tests for within-group comparisons of changes from baseline to final values.

[5] Excludes fried potatoes.

[6] Includes honey, candy or other added sugars.

[7] Excludes added animal fat.

Table 3—*Atherogenic lipoproteins and particles at baseline and 4-weeks*

	Baseline[1]	Final[1]	Change[2]	*P*[3]
Weight (kg)	108.1 ± 28.6	101.4 ± 26.3	-6% (-6.6 ± 3.6)	<0.0005
BMI (kg/m2)	37.5 ± 8.3	35.2 ± 7.8	-6% (-2.2 ± 1.1)	<0.0005
Total-C (mg/dL)	216.6 ± 34.2	182.7 ± 29.9	-16% (-33.8 ± 25.9)	<0.0005
LDL-C (mg/dL)	143.0 ± 28.9	118.4 ± 26.4	-17% (-24.6 ± 21.3)	<0.0005
HDL-C (mg/dL)	54.8 ± 9.4	49.5 ± 10.6	-9% (-5.2 ± 6.2)	<0.0005
Triglycerides (mg/dL)	124.1 ± 58.1	104.5 ± 53.6	-16% (-19.6 ± 38.4)	0.008
Lp(a) (nmol/L)[4]	200.7 ± 150.0	168.8 ± 126.7	-16% (-32.0 ± 52.3)	0.003
Apo-B (mg/dL)	115.2 ± 24.5	101.9 ± 17.7	-11% (-13.3 ± 18.3)	<0.0005
LDL-P (nmol/L)[5]	1891 ± 586	1586 ± 508	-16% (-305 ± 363)	<0.0005
*sd*LDL-C (mg/dL)	33.7 ± 11.5	23.7 ± 8.7	-30% (-10.0 ± 9.2)	<0.0005
HDL2-C (mg/dL)	17.4 ± 9.8	15.6 ± 9.9	-10% (-1.8 ± 4.5)	0.030
Apo A-1 (mg/dL)	189.7 ± 150.7	160.2 ± 126.5	-14% (-27.0 ± 19.6)	<0.0005

[1] Mean ± standard deviation (*n* =31 unless otherwise indicated)

[2] Data indicated as % change (mean ± standard deviation)

[3] Paired samples t-tests for within-group comparisons of changes from baseline to final values.

[4] n = 28 due to premature coagulation of sample (n=1) and incompatible units (mg/dL) when merging laboratory results (n=2).

[5] n = 29 due to premature coagulation of samples

List of abbreviations: BMI, body mass index; Total-C, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol;
Lp(a), lipoprotein(a); Apo-B, apolipoprotein B100; LDL-P, low-density lipoprotein particles;
sdLDL-C, small-dense low-density lipoprotein cholesterol;
HDL2-C, high-density lipoprotein-2 cholesterol; Apo A-1, apolipoprotein A-1.

Table 4—*Inflammatory and other cardiovascular indicators at baseline and 4-weeks*

	Baseline[1]	Final[1]	Change[2]	*P*[3]
hs-CRP (mg/dL)	7.8 ± 6.4	5.4 ± 4.7	-30.7% (-2.4 ± 3.7)	0.001
Endothelin (pg/mL)[4]	2.2 ± 0.7	2.2 ± 0.8	0% (0.0 ± 0.7)	0.916
IL-6 (pg/mL)[4]	2.6 ± 1.4	2.0 ± 1.0	-23.1% (-0.6 ± 1.0)	0.001
TNF-α (pg/mL)[4]	2.0 ± 0.9	2.2 ± 0.9	10.0% (0.2 ± 0.6)	0.096
Lp-PLA_2 (ng/mL)[4]	252.3 ± 136.3	210.7 ± 119.1	-16.4% (-41.6 ± 64.6)	0.001
Myeloperoxidase (pmol/L)[5]	124.1 ± 58.1	104.5 ± 53.6	-23.0% (-28.5 ± 66.1)	0.056
Fibrinogen (mg/dL)[6]	561.4 ± 112.2	530.1 ± 102.9	-5.6% (-31.3 ± 50.7)	0.004
NT-proBNP	65.2 ± 71.2	69.4 ± 75.9	6.2% (4.1 ± 23.2)	0.337
Total WBC (K/ul)[4]	6.3 ± 2.0	4.8 ± 1.3	-22.2% (-1.4 ± 1.1)	<0.0005
Neutrophils (K/ul)[4]	3.5 ± 1.4	2.5 ± 0.9	-28.6% (-1.0 ± 0.8)	<0.0005
Lymphocytes (K/ul)[4]	1.9 ± 0.7	1.6 ± 0.6	-15.8% (-0.3 ± 0.4)	<0.0005
Monocytes (K/ul)[4]	0.46 ± 0.12	0.38 ± 0.09	-15.2% (-0.07 ± 0.1)	<0.0005
Eosinophils (K/ul)[4]	0.18 ± 0.11	0.15 ± 0.11	-16.6% (-0.03 ± 0.07)	0.033
Basophils (K/ul)[4]	0.029 ± 0.016	0.024 ± 0.015	-17.2% (-0.005 ± 0.010)	0.016

[1] Mean ± standard deviation (*n*=31 unless otherwise indicated)

[2] Data indicated as % change (mean ± standard deviation)

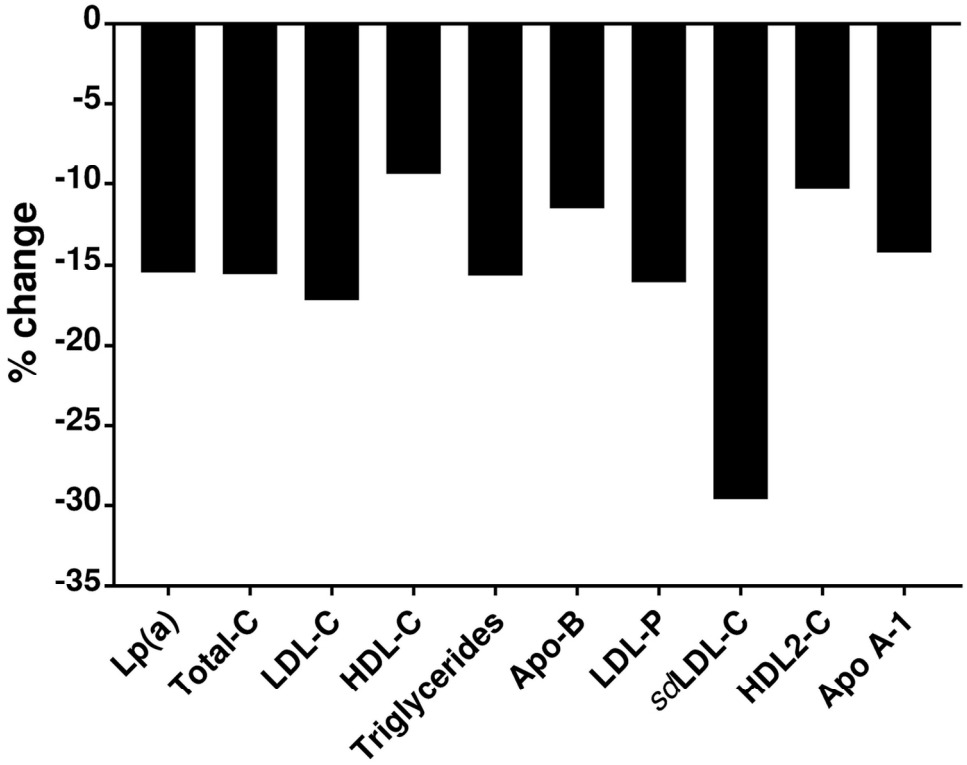
[3] Paired samples t-tests for within-group comparisons of changes from baseline to final values.

[4] n = 30 due to premature coagulation of samples

[5] n = 25 due to premature coagulation of samples

[6] n = 27 due to premature coagulation of samples

List of abbreviations: *hs*-CRP, high-sensitivity c-reactive protein; IL-6, interleukin-6; TNF-α, tumor necrosis factor-alpha; Lp-PLA_2, lipoprotein-associated phospholipase A2; NT-proBNP, N-terminal pro b-type natriuretic peptide; WBC, white blood cells.



Percent change of atherogenic lipoproteins and particles from baseline to 4-weeks. All variable changes indicated are significant ($P < 0.05$).

List of abbreviations: Lp(a), lipoprotein(a); Total-C, total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; Apo-B, apolipoprotein B100; LDL-P, low-density lipoprotein particles; sdLDL-C, small-dense low-density lipoprotein cholesterol; HDL2-C, high-density lipoprotein-2 cholesterol; Apo A-1, apolipoprotein A-1.