Published in final edited form as:
Nutr Metab Cardiovasc Dis. 2013 September ; 23(9): 857–863. doi:10.1016/j.numecd.2012.05.003.

Relationships Among Changes in C-Reactive Protein and Cardiovascular Disease Risk Factors With Lifestyle Interventions

D. Young[a], **S. Camhi**[b], **T. Wu**[a], **J. Hagberg**[c], and **M. Stefanick**[d]

[a]Department of Epidemiology and Biostatistics, University of Maryland School of Public Health College Park, MD

[b]Department of Exercise and Health Science, University of Massachusetts, Boston, Boston MA

[c]Department of Kinesiology, University of Maryland School of Public Health, College Park, MD

[d]Stanford Prevention Research Center, Department of Medicine, Stanford University School of Medicine, Stanford, CA

Abstract

Background and Aims—Inflammation plays a role in the development of cardiovascular disease (CVD). Elevated levels of the inflammatory marker, C-reactive protein (CRP), are cross-sectionally associated with traditional CVD risk factors and are being considered as an emerging CVD risk factor. In a secondary data analysis, we examined changes in CRP and several CVD risk factors after one-year diet and exercise interventions to assess whether CRP changed concurrently with other risk factors, or was independent of the traditional risk factors.

Methods and Results—Data were analyzed from 143 men and 133 women with dyslipidemia who were randomized to one-year interventions of low-fat diet only, physical activity only, diet plus physical activity, or control. Plasma high-sensitivity CRP, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, triglycerides (TG), fasting and 2-hr blood glucose and insulin, blood pressure (BP), and waist circumference were obtained at baseline and follow-up. Multiple linear regression models were used to predict CRP change based on other risk factor changes, controlling for age, race, alcohol intake, and hormone replacement therapy. Treatment groups were combined for analysis. Baseline mean (SD) CRP levels were 1.3±1.3 (men) and 1.9±1.8 mg/L (women), with mean changes of -0.11±1.3 and -0.17±1.5 mg/L, respectively. Plasma CRP change was negatively associated with TG change in men (p=0.003) and women (p=0.05), positively associated with change in systolic BP in men (p=0.01), but was not associated with changes in the other risk factors.

Conclusion—Dietary and/or physical activity induced changes in CRP may be largely independent of traditional CVD risk factors in persons with dyslipidemia.

Corresponding author: Deborah Rohm Young, PhD, Department of Research and Evaluation, Kaiser Permanente Southern California Medical Group, 100 S. Los Robles, 2nd Floor, Pasadena, CA 91101. 626-564-3887 (phone) 626-564-3409 (fax) deborah.r.young@kp.org.

Keywords

C-reactive protein; cardiovascular disease risk; physical activity; low-fat diet; interventions

Introduction

Inflammation plays a significant role in the pathogenesis of atherosclerosis and the resultant cardiovascular disease (CVD) [1]. There is also evidence that inflammation is involved in the development of type 2 diabetes [2], metabolic syndrome [3], and metabolic syndrome precursors such as insulin resistance and hyperglycemia [4]. C-reactive protein (CRP), an acute-phase reactant, is a non-sensitive marker of inflammation. It may be able to provide additional information over traditional CVD risk factors to identify those at risk for developing CVD [5], although the biological mechanisms that would demonstrate an independent association are not fully understood. It may contribute to the development of atherosclerotic disease and, hence, directly enhance this process; however, it is also possible that CRP may only be a marker of the inflammatory activity occurring in the lesions [6]. Thus, it is currently not clear whether CRP is a risk factor or a risk marker for CVD.

Cross-sectional analyses have repeatedly found that CRP levels are positively associated with blood pressure (BP) [6,7], low-density lipoprotein (LDL-C) and total cholesterol [4,7], fasting glucose [8], and triglyceride (TG) levels [6,7], and negatively associated with high-density lipoprotein cholesterol (HDL-C) levels [4,6,7]. However, there is little information on whether changes in traditional CHD risk factors are associated with change in CRP. One study that assessed the effect of a low-fat diet weight loss program on CRP found that CRP levels were not associated with change in lipids or glucose [9]. More information is needed to better understand the relationship of changes in CHD risk factors and emerging risk factors, such as CRP, with drug or lifestyle interventions.

We previously found that plasma CRP levels decreased significantly in response to a diet and a diet plus physical activity intervention in women with metabolic syndrome, but no change in CRP levels was found in men [10]. In the present study, we examined the relationships between change in CRP and changes in CHD risk factors in a secondary analysis of the Diet and Exercise for Elevated cardiovascular disease Risk (DEER) trial [11]. This data set is ideal for examining change in CRP and CVD risk factors because these interventions have previously been shown to result in a number of beneficial effects on CHD risk factors [11] and a high-quality diet and physical activity may improve CRP [12,13]. We hypothesized that a decrease in BP and LDL-C and an increase in HDL-C would be associated with decreases in CRP.

Methods

Study Population

The original DEER trial tested the effects of implementing a low-fat diet and physical activity program individually and combined on plasma lipoprotein-lipid levels in individuals with abnormal lipid profiles (i.e., low HDL-C and elevated LDL-C levels). Since HDL-C levels are considered a CVD risk factor that differ for men and women, eligibility criteria for men and women differed in the original DEER trial. Men between the years of 30 and 64 meeting the following criteria were eligible: HDL-C <45 mg/dL, plasma LDL-C of 126-189 mg/dL, and BMI <34 kg/m^2. Women had to be post-menopausal and between the ages of 45 and 65 with HDL-C levels <60 mg/dL, LDL-C levels of 126-209 mg/dL, and BMI <32 kg/m^2. Other recruitment criteria for both sexes included resting BP <160/95 mmHg, TG levels <500 mg/dL, fasting blood glucose <140 and <200 mg/dL after an oral glucose load, and

normal results from a maximal treadmill exercise test. Exclusion criteria included history of CVD, stroke, diabetes, cancer, or any other life-threatening illness, or current use of insulin, BP, lipid-lowering or cardiac medications [11]. Participants were not required to be sedentary or consume an unhealthful diet. The trial was approved by the Institutional Review Board of the Stanford University School of Medicine and participants provided written informed consent. The secondary data analysis performed for this report was approved by the University of Maryland Institutional Review Board.

Individuals underwent assessments prior to randomization and again at the end of the one-year trial. The same procedures were used to obtain baseline and follow-up measures. Participant demographics and usual alcohol intake (drinks per week) were assessed from a self-report survey. Stature was determined from a Harpenden stadiometer and body mass from a standard beam balance; BMI was calculated as weight in kg/height in m^2. Body density was determined using standard equations from Jackson and Pollock based on 3 different skinfold sites in men and women [14,15]. These equations were developed in large populations using underwater weighing as the criterion measure and were subsequently validated in large independent cohorts. The Siri equation was used to calculate percent body fat [16]. BP was manually measured over the brachial artery using a mercury sphygmomanometer after a 5-min seated rest; two assessments were obtained and the mean was calculated. Venous blood was obtained on two separate visits at baseline and one visit at follow-up. Participants consumed 75 g of glucose after fasting blood samples were collected. After two hours, blood was drawn to determine glucose tolerance. Fasting and 2-hour insulin levels were also obtained. Blood samples were centrifuged and plasma was stored in a -80° C freezer. For all assessments, participants were asked to fast for at least 12 hours and abstain from vigorous physical activity and alcohol consumption for at least 24 hours and from smoking for 1 hour.

Plasma high sensitivity CRP (hs-CRP) was measured in frozen plasma using a high-sensitivity immunoturbidimetric assay using a Hitachi 917 analyzer (Roche Diagnostics, Indianapolis, IN) using reagents and calibrators from DiaSorin (Stillwater MN). This assay has a sensitivity of 0.03 mg/L, with day-to-day variability of 2.81%, 1.61%, and 1.1% at concentrations of 0.91, 3.07, ad 13.38 mg/mL, respectively. Plasma cholesterol and TG levels were measured using standard enzymatic techniques. Plasma HDL-C levels were measured using dextran sulfate-magnesium precipitation and subsequent enzymatic measurement of non-precipitated cholesterol. Very low-density lipoprotein cholesterol (VLDL-C) was calculated and LDL-C was then calculated as total cholesterol minus HDL-C and VLDL-C. Plasma glucose was analyzed by the National Health Laboratories (San Diego, CA). Insulin was assessed using standard measures. Plasma lipoprotein-lipids, glucose, and insulin were analyzed in 1994; CRP was analyzed in 2007. The samples had not been thawed during this interval. CRP is highly stable when frozen at -70°C for periods up to 20 years [17]. Each participant's baseline and follow-up sample for CRP levels were measured in the same assay to minimize the effects of inter-assay variation. One specimen was available for measurement at each time point.

In the original DEER trial eligible participants were randomized to four groups: low-fat diet only, physical activity only, combined low-fat diet and physical activity, and control [11]. Participants randomized to the low-fat diet and low-fat diet plus physical activity groups were provided with recommendations to adopt the National Cholesterol Education Program Step 2 diet [18]. Participants attended an individualized counseling session with a registered dietitian, followed by eight group sessions to promote the dietary recommendations of <30% of total calories from fat, <7% from saturated fat, and < 200 mg of cholesterol/day. Group sessions addressed ways to replace fat with complex carbohydrates, low-fat dairy products, and lean meats. The initial twelve-week adoption phase was followed by a six- to eight-

month maintenance phase with monthly in-person, group, telephone, or mail contacts. Weight loss was not emphasized. Participants in the diet-only group were asked to maintain their current physical activity levels throughout the intervention period.

The goal in the physical activity and physical activity plus low-fat diet intervention groups was for participants to engage in moderate-to-vigorous aerobic physical activity at a level equivalent to at least 10 miles/week of brisk walking or jogging. This intervention began with a one-on-one meeting with an exercise leader, followed by a six-week adoption phase of supervised group exercise three times per week. A 7-8 month maintenance phase followed during which participants could continue supervised group physical activity, continue physical activity at home, or participate in a combination of group and home-based programs. Participants in the physical activity-only treatment group were asked to maintain their current dietary habits. Weight loss was not emphasized.

A total of 197 men and 181 women participated in the DEER trial. After eliminating individuals who had missing CRP levels, missing CVD risk factor data, or initial CRP values >10 mg/dL [19] (less than 10 participants), the sample used for this study consisted of 143 men and 133 women. As we were interested in the relationships between changes in CRP levels and CVD risk factors over the 1 year study time frame, and not specifically with the different interventions, all individuals were collapsed into one group for the primary analysis. Secondary analyses examined potential within treatment group associations.

Changes in CRP levels and the other risk factors were calculated as final minus initial values. Multiple linear regression models were fit to predict change in CRP based on CVD risk factor changes, with age, race (white or other race), and alcohol intake, and the other CVD risk factors included as covariates. The Framingham Risk Score, a composite score for CVD risk [20], was calculated and change analyzed using the same procedures, but because the score contains several CVD risk factors, it was not included in the regressions. Hormone replacement therapy use was controlled in the analysis for women. We conducted similar analyses within each treatment group. Finally, participants were categorized based on their baseline CRP levels (i.e., low < 1.0 mg/L; average 1.0–3.0 mg/L; high >3.0 to 10 mg/L) [19] and CVD risk factor baseline levels and changes within these subgroups were compared using one-way ANOVA. Data were analyzed using SAS version 9.1 (SAS Institute, Cary NC) and statistical significance was set at $P < 0.05$.

Results

Participants were mostly white (85%), non-smokers (no men and 4 women smoked), and most consumed less than 1 alcohol drink per day [10]. Baseline risk factors were consistent with the original DEER trial design; participants had low HDL-C and elevated LDL-C, and TG levels (Table 1). Body composition measures suggest participants were generally overweight but not obese. BP and fasting and 2-hour glucose and insulin levels were within normal ranges. Mean CRP levels placed participants at average CVD risk, although 11% of men and 18% of women had baseline CRP levels in the high category. The average changes for all of the CVD risk factors and CRP were in the favorable direction (Table 2).

The results from the multivariate regression analyses are displayed in Table 3. For men, change in systolic BP and TG was significantly associated with change in CRP. For women, only the relationship between the change in TG and CRP was significant. Change in the Framingham risk score was not associated with change in CRP in either sex (data not shown).

Regression analyses by treatment group status indicated several significant results in three of the eight groups. For men in the diet plus physical activity group assignment change in CRP

was associated with change in percent body fat (regression coefficient [SE] 0.270 [0.11], P=0.02), change in 2-hour glucose (-0.03 [0.01], P=0.02), and change in fasting insulin (-0.20 [0.08], P-0.03). For women in the delayed intervention, change in CRP was associated with change in systolic BP (-0.14 [0.06], P=0.04). For women in the diet group, change in CRP was associated with change in waist circumference (0.16 [0.06], P=0.05).

We examined these relationships further by determining if the changes in CVD risk factors differed across initial CRP risk categories. There were significant differences in baseline levels of CVD risk factors across CRP risk categories (Table 4), including BMI, percent fat, waist circumference, systolic and diastolic BP, fasting and 2-hour glucose, and 2-hour insulin in women, and BMI, percent fat, waist circumference, and LDL-C for men. No significant differences were found for change in CVD risk factors or Framingham risk score across baseline CRP risk categories.

Discussion

We found that CRP change was not concomitant with the changes in most of the traditional CVD risk factors or the Framingham risk score following diet and physical activity interventions. In the combined group analyses, the only significant co-occurring changes with CRP were noted for systolic BP and TG in men and for TG in women. Within-treatment group analyses found associations for change in CRP and change in percent fat, waist circumference, systolic BP, glucose, and insulin, which were mostly in unexpected directions except for the body composition variables. These results suggest that the CVD and CRP changes resulting from these lifestyle interventions may be largely independent.

Accumulating evidence suggests that plasma CRP levels may independently predict CVD risk. Ridker and colleagues demonstrated that within both Framingham risk score categories and LDL-C categories, lower CRP levels were associated with lower risk of CVD events [21]. Women with low LDL-C but high CRP were at higher risk than those with high LDL-C but low CRP. Tuomisto et al. found that after adjusting for traditional CVD risk factors, baseline plasma CRP levels predicted CVD events and total mortality in men, but not women [22]. Data from the Framingham Heart Study demonstrated that including high CRP in the risk prediction equation along with traditional CVD risk factors provided an 11.8% improvement in predicting coronary heart disease outcomes [23]. Others have found high plasma CRP levels to independently predict ischemic stroke [24].

The present study used diet and physical activity interventions to alter CVD risk factors and CRP, whereas others examining this relationship have intervened with statin therapy. Nissen et al. randomized participants with coronary artery disease to statin treatment and examined CRP and lipid change [25]. They found changes in LDL-C of a magnitude 10-fold greater than ours (LDL-C change -63 ± 44 compared with -7 ± 25 (men and women combined)); however CRP change was similar (-0.2 [interquartile range -1.9 to 0.8] vs -0.14 ± 1.4, Nissen et al and our results, respectively). The association between change in LDL-C and CRP was modest, but statistically significant (r = 0.13). They suggest that the statin-mediated reduction in CRP is not likely to be a consequence of LDL-C change, but rather from an independent statin effect on CRP [25]. Given the financial and quality of life costs associated with lifelong use of statin therapy and the low magnitude of change in CRP levels, more effort should be placed in promoting lifestyle changes for CRP reduction.

We found direct associations between change in systolic BP and change in CRP for men. Pravenec and colleagues transgenically expressed human CRP in spontaneously hypertensive rats and demonstrated that increased expression of the human CRP gene increased BP, TG, and insulin response to a glucose tolerance test [26]. Their data suggest

that increased CRP may attenuate nitric oxide availability, which may result in increased BP and a deterioration of glucose and insulin metabolism. An animal model allows researchers to examine potential mechanisms by which CRP may contribute to pathogenesis, but more work is necessary to translate these results to humans. Nonetheless, the results suggesting that increased CRP may result in higher BP needs exploration.

We did not expect to find a negative association between change in CRP and TG. Two of the interventions included a low-fat diet, which is beneficial for lowering LDL-C but can result in increased TG levels [27]. The DEER trial found a lower magnitude of TG change for the diet only and diet plus exercise groups although there were no significant between-group differences in plasma TG changes [11]. Testing a similar dietary intervention of 27% total fat and 6% saturated fat, Erlinger et al. found that plasma TG levels increased in participants with high CRP levels [28]. We also found that TG increased in men and women with elevated CRP levels (≥ 3 mg/L), but only 11% of men and 18% of women in our sample initially had high CRP levels. It is possible that inflammation, evidenced by high CRP levels, may be a marker or determinant of an adverse TG response to a low-fat diet [28].

This study has a number of strengths. We had sufficient sample size to analyze the results separately for men and women. This is important, as it is well-documented that women have higher CRP levels than men [29] and thus, may have a different response to lifestyle interventions in terms of CRP levels. The sample was not taking any medications that could alter other CVD risk factors and perhaps attenuate any potential associations between the changes in CRP levels and CVD risk factors. We controlled for known influences on CRP levels. Given the established influence of weight status and change in weight on CRP levels [30] and traditional CVD risk factors, it is notable that change in percent body fat was not associated with CRP change.

The study also has limitations. Participants were at high risk for developing CVD given their dyslipidemic status. Our results may not be consistent when tested in participants with different cardiometabolic profiles. Even though our participants were dyslipidemic, most had initial CRP levels in the low or average categories. This study was a secondary analysis of a trial that was designed for different primary outcomes.

In conclusion, we found that change in plasma CRP was largely independent of change in most other traditional CVD risk factors in this at-risk, dyslipidemic population after 1-year diet and physical activity interventions. Our results provide some evidence that CRP may be largely independent from traditional CVD risk factors in persons with dyslipidemia.

Acknowledgments

This work was funded by a grant from the National Institutes of Health, R21 HL086651.

Reference List

1. Ross R. Atherosclerosis is an inflammatory disease. Am Heart J. 1999; 138:S419–S420. [PubMed: 10539839]
2. Duncan BB, Schmidt MI, Pankow, et al. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. Diabetes. 2003; 52:1799–805. [PubMed: 12829649]
3. Ridker PM, Buring JE, Cook NR, Rifai N. C-reactive protein, the metabolic syndrome, and risk of incident cardiovascular events: an 8-year follow-up of 14 719 initially healthy American women. Circulation. 2003 Jan 28; 107(3):391–7. [PubMed: 12551861]

4. Aronson D, Bartha P, Zinder O, et al. Association between fasting glucose and C-reactive protein in middle-aged subjects. Diabet Med. 2004; 21:39–44. [PubMed: 14706052]
5. Pearson TA, Bazzarre TL, Daniels SR, et al. American Heart Association guide for improving cardiovascular health at the community level: a statement for public health practitioners, healthcare providers, and health policy makers from the American Heart Association Expert Panel on Population and Prevention Science. Circulation. 2003; 107:645–51. [PubMed: 12566381]
6. Fredrikson GN, Hedblad B, Nilsson JA, Alm R, Berglund G, Nilsson. Association between diet, lifestyle, metabolic cardiovascular risk factors, and plasma C-reactive protein levels. Metabolism. 2004; 53:1436–42. [PubMed: 15536598]
7. Miller M, Zhan M, Havas S. High attributable risk of elevated C-reactive protein level to conventional coronary heart disease risk factors: the Third National Health and Nutrition Examination Survey. Arch Intern Med. 2005; 165:2063–8. [PubMed: 16216995]
8. Danesh J, Wheeler JG, Hirschfield GM, et al. C-reactive protein and other circulating markers of inflammation in the prediction of coronary heart disease. N Engl J Med. 2004; 350:1387–97. [PubMed: 15070788]
9. Heilbronn LK, Noakes M, Clifton PM. Energy restriction and weight loss on very-low-fat diets reduce C-reactive protein concentrations in obese, healthy women. Arterioscler Thromb Vasc Biol. 2001; 21:968–70. [PubMed: 11397705]
10. Camhi SM, Stefanick ML, Ridker PM, Young DR. Changes in C-reactive protein from low-fat diet and/or physical activity in men and women with and without metabolic syndrome. Metabolism. 2010; 59:54–61. [PubMed: 19709693]
11. Stefanick ML, Mackey S, Sheehan M, Ellsworth N, Haskell WL, Wood PD. Effects of diet and exercise in men and postmenopausal women with low levels of HDL cholesterol and high levels of LDL cholesterol. N Engl J Med. 1998; 339:12–20. [PubMed: 9647874]
12. Esposito K, Marfella R, Ciotola M, et al. Effect of a mediterranean-style diet on endothelial dysfunction and markers of vascular inflammation in the metabolic syndrome: a randomized trial. JAMA. 2004; 292:1440–6. [PubMed: 15383514]
13. Ford ES. Does exercise reduce inflammation? Physical activity and C-reactive protein among U.S. adults. Epidemiology. 2002; 13:561–8. [PubMed: 12192226]
14. Jackson AS, Pollock ML, Ward A. Generalized equations for predicting body density of women. Med Sci Sports Exerc. 1980; 12:175–81. [PubMed: 7402053]
15. Jackson AS, Pollock ML. Generalized equations for predicting body density of men. 1978. Br J Nutr. 2004; 91:161–8. [PubMed: 14748950]
16. Siri, W. Body composition from fluid spaces and density - analysis of methods. In: Brozek, J.; Henschel, A., editors. Techniques for measuring body composition. Washington, DC: National Academy of Sciences; 1961. p. 223-44.
17. Wilkins J, Gallimore JR, Moore EG, Pepys MB. Rapid automated high sensitivity enzyme immunoassay of C-reactive protein. Clin Chem. 1998; 44:1358–61. [PubMed: 9625071]
18. Summary of the second report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II). JAMA. 1993; 269:3015–23. [PubMed: 8501844]
19. Myers GL, Rifai N, Tracy RP, et al. CDC/AHA Workshop on Markers of Inflammation and Cardiovascular Disease: Application to Clinical and Public Health Practice: report from the laboratory science discussion group. Circulation. 2004; 110:e545–e549. [PubMed: 15611379]
20. Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA. 2001; 285:2486–97. [PubMed: 11368702]
21. Ridker PM, Rifai N, Rose L, Buring JE, Cook NR. Comparison of C-reactive protein and low-density lipoprotein cholesterol levels in the prediction of first cardiovascular events. N Engl J Med. 2002; 347:1557–65. [PubMed: 12432042]
22. Tuomisto K, Jousilahti P, Sundvall J, Pajunen P, Salomaa V. C-reactive protein, interleukin-6 and tumor necrosis factor alpha as predictors of incident coronary and cardiovascular events and total mortality. A population-based, prospective study. Thromb Haemost. 2006; 95:511–8. [PubMed: 16525580]

23. Wilson PW, Pencina M, Jacques P, Selhub J, D'Agostino R Sr, O'Donnell CJ. C-reactive protein and reclassification of cardiovascular risk in the Framingham Heart Study. Circ Cardiovasc Qual Outcomes. 2008; 1:92–7. [PubMed: 20031795]
24. Ballantyne CM, Hoogeveen RC, Bang H, Coresh J, Folsom AR, Chambless LE, et al. Lipoprotein-associated phospholipase A2, high-sensitivity C-reactive protein, and risk for incident ischemic stroke in middle-aged men and women in the Atherosclerosis Risk in Communities (ARIC) study. Arch Intern Med. 2005; 165:2479–84. [PubMed: 16314544]
25. Nissen SE, Tuzcu EM, Schoenhagen P, Crowe T, Sasiela WJ, Tsai J, et al. Statin therapy, LDL cholesterol, C-reactive protein, and coronary artery disease. N Engl J Med. 2005; 352:29–38. [PubMed: 15635110]
26. Pravenec M, Kajiya T, Zidek V, Landa V, Mlejnek P, Simakova M, et al. Effects of human C-reactive protein on pathogenesis of features of the metabolic syndrome. Hypertension. 2011; 57:731–7. [PubMed: 21357282]
27. Katan MB, Grundy SM, Willett WC. Should a low-fat, high-carbohydrate diet be recommended for everyone? Beyond low-fat diets. N Engl J Med. 1997; 337:563–6. [PubMed: 9262504]
28. Erlinger TP, Miller ER III, Charleston J, Appel LJ. Inflammation modifies the effects of a reduced-fat low-cholesterol diet on lipids: results from the DASH-sodium trial. Circulation. 2003; 108:150–4. [PubMed: 12847067]
29. Albert MA, Ridker PM. C-reactive protein as a risk predictor: do race/ethnicity and gender make a difference? Circulation. 2006; 114:e67–e74. [PubMed: 16880331]
30. Selvin E, Paynter NP, Erlinger TP. The effect of weight loss on C-reactive protein: a systematic review. Arch Intern Med. 2007; 167:31–9. [PubMed: 17210875]

Table 1

Baseline values for study participants.

	Men (n=143)	Women (n=133)
Age (yr)	48.0±9.0	56.5±5.0
Body mass index (kg/m^2)	26.8±2.8	26.2±3.2
Percent body fat (%)	21.7±4.3	32.0±5.3
Waist circumference (cm)	95.4±8.9	84.5±9.2
Systolic BP (mm Hg)	113±12	115±14
Diastolic BP (mm Hg)	76±8	73±86
LDL-C (mg/dL)	157±17	165±21
HDL-C (mg/dL)	35±5	45±7
Triglycerides (mg/dL)	166±66	155±69
Fasting glucose (mg/dL)	96.1±8.6	93.9±8.8
2-hour glucose (mg/dL)	98.4±31.3	102.6±30.4
Fasting insulin (μU/mL)	15.1±10.9	12.7±11.2
2-hour insulin (μU/mL)	83.3±76.2	76.6±67.1
Framingham risk score	7.7±6.3	1.8±1.9
C-reactive protein (mg/L)	1.3±1.3	1.9±1.8
C-reactive protein low category	85 (59%)	49 (37%)
C-reactive protein average category	43 (30%)	60 (45%)
C-reactive protein high category	15 (11%)	24 (18%)

Data are expressed as mean ± SD. For the C-reactive protein category variables, the values are the percentages of that sex group that had initial plasma C-reactive protein levels in the low category (<1.0 mg/L), the average category (1.0 – 3.0 mg/L), or the high category (>3.0 mg/L).

Table 2

One-year change (year 1 – baseline) in cardiovascular disease risk factors for all study participants.

Variable	Men (n=143)	Women (n=133)
ΔBody mass index (kg/m^2)	-0.64±1.3	-0.51±1.5
ΔPercent body fat (%)	-1.02±3.5	-0.36±4.3
ΔWaist circumference (cm)	-3.5±4.6	-3.1±5.5
ΔSystolic BP (mmHg)	-0.75±8.8	-2.3±12.0
ΔDiastolic BP (mmHg)	-0.27±6.8	-2.1±6.7
ΔLDL-C (mg/dL)	-6.2±25.2	-7.8±23.9
ΔHDL-C (mg/dL)	0.63±5.1	0.93±7.5
ΔTriglycerides (mg/dL)	-3.2±69.2	-2.95±58.6
ΔFasting glucose (mg/dL)	-6.8±8.8	-6.3±11.7
Δ2-hour glucose (mg/dL)	-11.1±28.0	-4.8±25.3
ΔFasting insulin (μU/mL)	-2.5±10.2	-1.6±12.4
Δ2-hour insulin (μU/mL)	-18.9±55.3	-14.4±44.8
ΔFramingham risk score	-1.97±4.4	-0.44±1.6
ΔC-reactive protein (mg/L)	-0.11±1.3	-0.17±1.5

Data are expressed as mean ± SD of the change from baseline to follow-up. Abbreviations: BP, blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; Framingham risk score [20]

Table 3

Regression results evaluating associations between changes in cardiovascular disease risk factors and change in plasma C-reactive protein level.

	Men (n = 143)		Women (n = 133)	
Risk Factor	**Coefficient**	***P* Value**	**Coefficient**	***P* value**
Δ Percent body fat	0.018 (0.04)	0.64	-0.055 (0.04)	0.21
ΔWaist circumference	0.034 (0.03)	0.30	0.031 (0.04)	0.39
ΔSystolic BP	0.042 (0.02)	0.01	-0.023 (0.02)	0.14
ΔDiastolic BP	-0.026 (0.02)	0.18	-0.0023 (0.03)	0.94
ΔLDL-C	0.0007 (0.005)	0.89	-0.007 (0.007)	0.29
ΔHDL-C	-0.032 (0.03)	0.23	-0.004 (0.02)	0.86
ΔTriglycerides	-0.006 (0.002)	0.003	-0.005 (0.003)	0.05
ΔFasting glucose	-0.002 (0.01)	0.90	0.003 (0.01)	0.85
Δ2-hour glucose	-0.009 (0.005)	0.06	0.0009 (0.007)	0.91
ΔFasting insulin	0.004 (0.01)	0.78	0.021 (0.02)	0.38
Δ2-hour insulin	0.002 (0.002)	0.34	0.007 (0.004)	0.11

Analyses controlled for the variables in the table, age, race (white or not), alcohol intake, and change in percent body fat. For women, analyses also controlled for hormone replacement therapy. Values in parentheses for the coefficients are the SE. Abbreviations: BP, blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; Framingham risk score [20]

Nutr Metab Cardiovasc Dis. Author manuscript; available in PMC 2014 September 01.

Table 4

Levels of baseline cardiovascular risk factors and their changes across baseline C-reactive protein categories.

		Men				Women			
		Low CRP <1.0 mg/L (n=85)	**Average CRP 1-3 mg/L (n=43)**	**High CRP >3 mg/L (n=15)**	***P* value**	**Low CRP <1.0 mg/L (n=49)**	**Average CRP 1-3 mg/L (n=60)**	**High CRP >3 mg/L (n=24)**	***P* value**
Body mass index (kg/m2)	Baseline	26±3	27±3	28±3	0.05	24±3	27±3	28±3	<0.0001
	Change	-0.6±1	-0.7±1	-0.5±1	0.94	-0.5±2	-0.6±1	-0.4±1	0.87
Percent body fat (%)	Baseline	21±4	22±4	25±5	0.01	29±5	34±5	34±5	<0.0001
	Change	-1.4±4	-0.3±3	-0.9±3	0.29	-0.9±5	-0.6±4	1.2±4	0.14
Waist circumference (cm)	Baseline	94±9	97±9	100±9	0.03	80±9	87±8	89±8	<0.001
	Change	-3.5±4	-3.5±5	-3.4±4	0.99	-3.1±7	-3.3±5	-2.6±4	0.85
Systolic BP (mmHg)	Baseline	114±10	113±14	112±11	0.90	112±13	119±14	110±13	0.01
	Change	-2±9	1.2±9	1±9	0.08	-3±12	-3±12	2±12	0.15
Diastolic BP (mmHg)	Baseline	76±7	75±9	77±7	0.53	71±7	75±8	71±7	0.03
	Change	-0.9±7	0.5±7	1.3±7	0.37	-2.4±7	-2.3±7	-1±6	0.66
LDL-C (mg/dL)	Baseline	155±16	162±19	153±15	0.04	166±23	165±21	163±20	0.90
	Change	-5±25	-8±26	-7±22	0.89	-11±24	-8±22	-1±27	0.26
HDL-C (mg/dL)	Baseline	35±5	35±5	32±4	0.07	45±7	45±8	44±8	0.59
	Change	0.1±5	1.4±5	1.4±5	0.36	0.7±8	1.0±8	1.2±6	0.96
Triglycerides (mg/dL)	Baseline	171±71	157±62	166±48	0.54	139±76	160±64	176±65	0.07
	Change	-8±70	-3±65	22±77	0.32	-1±64	-6±52	2±63	0.86
Fasting glucose (mg/dL)	Baseline	97±9	95±9	95±6	0.64	91±7	96±9	95±11	0.03
	Change	-7.5±9.7	-5.7±7.6	-5.9±6.4	0.51	-6.1±10	-8.1±8.5	-2±19	0.10
2-hour glucose (mg/dL)	Baseline	98±32	100±32	94±25	0.82	95±31	104±31	115±25	0.03
	Change	-15±27	-9±30	2.1±24	0.09	-6±23	-3.3±28	-6.1±22	0.84
Fasting insulin (μU/mL)	Baseline	14±5	17±18	16±9	0.42	10±2.4	15±16	12±3	0.07
	Change	-2.2±4	-4.5±17	1.4±6	0.14	1.1±10	-3.5±16	-1.9±4	0.17
2-hour insulin (μU/mL)	Baseline	74±56	100±105	88±78	0.18	58±40	84±74	95±85	0.04
	Change	-17±48	-27±71	-7±44	0.40	-12±26	-13±56	-23+45	0.58
Framingham risk score	Baseline	7±6	9±7	7±6	0.51	2±2	2±2	1±1	0.12
	Change	-1.8±5	-2.4±4.2	-1.2±4	0.62	-0.4±1	-0.6±2	-0.1±1	0.49

Abbreviations: CRP, C-reactive protein BP, blood pressure; LDL-C, low-density lipoprotein cholesterol; HDL-C, high density lipoprotein cholesterol; Framingham risk score [20]