Can Exercise Training With Weight Loss Lower Serum C-Reactive Protein Levels?

Koichi Okita, Hirotaka Nishijima, Takeshi Murakami, Tatsuya Nagai, Noriteru Morita, Kazuya Yonezawa, Kenji Iizuka, Hideaki Kawaguchi, Akira Kitabatake

Objective—C-reactive protein (CRP), an obesity-related inflammatory marker, is a promising predictor for cardiovascular disease and may be a mediator for atherogenesis. It has been reported that diet-induced weight loss lowered CRP levels. However, the effect of exercise training, another therapy that can reduce weight, on CRP is still unclear. We examined effects of exercise training with weight loss on CRP levels and conventional cardiovascular risks.

Methods and Results—A total of 227 apparently healthy women were recruited, and 199 subjects (average age 52 years) completed a 2-month weight reduction program consisting of supervised aerobic exercises. After the program, weight was reduced from 65.8 to 62.8 kg (P<0.0001), and all conventional variables were remarkably improved. Similarly, CRP levels were significantly decreased, from 0.63 (0.28 to 1.19) to 0.41 (0.18 to 0.80) mg/L (P<0.0001). However, in contrast to other variables, the changes in CRP levels were not disproportionately associated with the extent of weight reduction. In the quartile analysis of % weight reduction, the largest weight reduction quartile did not show significant decreases in CRP levels, whereas moderate quartile showed remarkable CRP decreases.

Conclusions—Exercise training with weight reduction disproportionately lowered CRP levels. Considering inflammatory status, there might be an optimal pace of exercise with weight loss. (Arterioscler Thromb Vasc Biol. 2004;24:1-7.)

Key Words: C-reactive protein ■ atherosclerosis ■ inflammation ■ obesity ■ risk factors ■ exercise
supervised exercise training, subjects were recommended to perform home-based exercise ≥ 1 days a week. Only at the baseline examination did dieticians make simple nutritional education suitable for exercise training to the subjects.

**Clinical and Anthropometric Measurements**

At baseline and after the weight reduction program, subjects came to our institution to provide data on blood, physical measurements, muscle strength, and exercise tolerance. Exercise tolerance was estimated by electromechanical bicycle ergometer with an incremental protocol (25 W/2 minutes) and expressed as calculated peak oxygen uptake. Thigh strength was measured by an Anaeropress 3500 (Combi). Measurements of waist (narrowest circumference viewed from the front) and hip (largest horizontal circumference around the buttocks) were recorded. Abdominal wall fat (maximal thickness of perirenal fat at the anterior surface of the liver) and thigh muscle thickness at the anterior middle portion between the knee and the anterior crest of the ilium were evaluated with ultrasound tomography. Resting heart rate and blood pressure were measured. ECG and chest x-ray film were also examined.

**Laboratory Measurements**

Fasting venous blood samples were collected at the same time in the morning, after subjects had abstained from all food and drink, except water, for at least 12 hours, and from vigorous activity also for at least 12 hours. Fasting total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides, glycohemoglobin A1c (HbA1c), insulin, and glucose levels were measured. In addition, white blood cell count (WBC), uric acid, and liver function profiles such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), and γ-glutamyl transpeptidase (γ-GTP) were also measured. Insulin sensitivity was calculated by using the homeostasis assessment model (HOMA-R), a mathematical estimate of insulin sensitivity based on fasting glucose and insulin concentrations. Serum high-sensitivity CRP and amyloid A protein (SAA) levels were measured by a latex-enhanced immunonephelometric assay.

**Statistical Analysis**

Statistical analysis was performed using Statview 5.0 (SAS Institute). The 2-sided t test for paired samples was used to determine the significance of differences between several measurements before and after the weight reduction program. The significance of any differences in medians for paired data were evaluated with a nonparametric Wilcoxon signed rank sum test. Spearman rank correlation coefficients were used to quantify the correlations. In the quartile analysis, effects of exercise training on variables within each quartile were evaluated in the manner described above for paired data. Data are presented as mean (SD) or as median (interquartile range) for skewed variables. Significance levels are shown for all comparisons and relationships where P<0.05.

**Results**

The baseline physical and metabolic characteristics of the subjects are described in Table 1. Body mass index (BMI) ranged from 20.4 to 39.0 kg/m²; 186 subjects (82%) had a BMI >25 kg/m². The CRP levels were lower than those found in other studies of healthy women, although there were differences in BMI and dyslipidemic profiles among the studies.10,16,17 Univariate analysis by Spearman rank correlation coefficients between CRP levels and variables are shown in Table 2. The CRP levels were positively associated with obesity measures. On the other hand, CRP levels were inversely correlated with thigh strength and exercise tolerance. Similarly, all laboratory variables were significantly correlated with CRP levels. According to the univariate analysis, BMI, minimum waist girth, diastolic blood pressure, total/HDL cholesterol ratio, HDL cholesterol, triglycerides, HOMA-R, fasting glucose, uric acid, and ALT were selected for a stepwise regression with a forced entry of age. WBC and SAA were considered not appropriate for the model because they appear to be partially co-regulated with CRP through inflammatory mediators. In this multivariate analysis, BMI, total/HDL cholesterol ratio, ALT, and diastolic blood pressure were found to be independent factors relating to CRP levels.

Physical and metabolic characteristics at baseline and after a 2-month weight reduction program are shown in Table 3. Effects of exercise training were similarly obtained in premenopausal and postmenopausal women. Body weight was substantially reduced by 3.0 (1.9) kg, representing 4.6 (2.9)% of initial weight in total subjects. Other obesity measures were also significantly reduced. On the other hand, thigh

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**TABLE 1. Baseline Physical and Metabolic Characteristics in 227 Japanese Women**

<table>
<thead>
<tr>
<th>Variable</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>52 (10)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>155.3 (5.4)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>66.1 (8.4)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.4 (3.2)</td>
</tr>
<tr>
<td>Abdominal wall fat, mm</td>
<td>32.8 (9.0)</td>
</tr>
<tr>
<td>Minimum waist girth, cm</td>
<td>81.8 (7.6)</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.83 (0.06)</td>
</tr>
<tr>
<td>Thigh muscle thickness, mm</td>
<td>34.2 (6.1)</td>
</tr>
<tr>
<td>Resting heart rate, bpm</td>
<td>77 (10)</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>128 (18)</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>79 (10)</td>
</tr>
<tr>
<td>White blood cell count, 10⁹/L</td>
<td>5.0 (1.1)</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>224 (32)</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>138 (28)</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>64 (14)</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>91 (67–128)</td>
</tr>
<tr>
<td>Total/HDL cholesterol ratio</td>
<td>3.7 (0.9)</td>
</tr>
<tr>
<td>Fasting glucose, mg/dL</td>
<td>99 (15)</td>
</tr>
<tr>
<td>Fasting insulin, μU/mL</td>
<td>9.1 (6.3–13.7)</td>
</tr>
<tr>
<td>HOMA-R</td>
<td>2.1 (1.5–3.5)</td>
</tr>
<tr>
<td>Hemoglobin A1c, %</td>
<td>5.2 (0.4)</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>4.8 (1.0)</td>
</tr>
<tr>
<td>AST, IU/L</td>
<td>24 (11)</td>
</tr>
<tr>
<td>ALT, IU/L</td>
<td>26 (18)</td>
</tr>
<tr>
<td>γ-GTP, IU/L</td>
<td>31 (24)</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>0.60 (0.26–1.16)</td>
</tr>
<tr>
<td>Serum amyloid A protein, μg/mL</td>
<td>5.0 (3.4–8.2)</td>
</tr>
<tr>
<td>Peak oxygen uptake, ml/min per kg</td>
<td>21.9 (3.9)</td>
</tr>
<tr>
<td>Thigh strength, Watt/kg</td>
<td>11.7 (3.4)</td>
</tr>
</tbody>
</table>

Variables are presented as mean (SD), or as median (interquartile range) for skewed variables. LDL denotes low-density lipoprotein; HDL, high-density lipoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transpeptidase.
muscle thickness was unchanged. These findings indicated that only body fat, but not muscle mass, was reduced by this weight reduction program. Fitness status variables were improved, and all of the laboratory variables except HDL cholesterol were improved after the program. The absence of any improvement in HDL cholesterol after the program could be because of altered lipase activity during active phase of weight loss. Although HDL cholesterol was reduced, total/HDL cholesterol ratio was significantly improved. Similarly, significant reduction in CRP, SAA, and WBC levels was also observed after the program. Although CRP (P<0.05) and SAA (P<0.01) levels at baseline were significantly higher in postmenopausal women than in premenopausal women, effects of exercise training on obesity measures, fitness status, traditional risks, and inflammatory markers were similar between premenopausal and postmenopausal women.

The correlations between the extent of weight reduction and waist reduction (% to initial value) and variables are shown in Table 4. Waist reduction was not related to most of the changes in studied variables except waist-hip ratio and WBC. Although waist girth potentially relates to visceral fat, its change may be affected not only by reduction in visceral fat but also by abdominal muscle fitness and an accidental error in measurement. On the other hand, weight reduction was significantly associated with improvements in obesity measures, fitness status, blood pressure, lipid profiles, FBS, insulin, and HOMA-R. However, changes in CRP, SAA, and uric acid were not significantly correlated with the extent of weight reduction. Additionally, no significant correlation between changes in CRP and body weight was seen in premenopausal women (n=91, r=0.19, P=0.06) or especially in postmenopausal women (n=108, r=−0.07, P=0.47).

To further examine the relationship between the extent of weight reduction and the changes in variables, data were observed according to weight reduction quartiles (Figure). Subjects were divided on the basis of % weight reduction to initial weight. Mean weight reduction in the various groups was as follows: group A, −0.8 (0.8) kg, −1.1 (1.2) %; B, −2.3 (0.4) kg, −3.5 (0.5) %; C, −3.5 (0.6) kg, −5.4 (0.7) %; and D, −5.4 (1.1) kg, −8.4 (1.6) %. No significant differences in baseline characteristics were observed among quartile groups. Greater weight reduction corresponded to greater reduction in diastolic pressure, triglycerides, and fasting insulin. Other traditional risks showed a similar trend inconsistent with the results in Table 4; however, the pattern of CRP differed from that of those variables. The largest weight reduction group (D) did not show a proportional decrease in CRP levels corresponding to weight reduction. The SAA levels showed a similar trend. Interestingly, the serum uric acid levels were rather increased in group D, although this increase did not reach statistical significance (P=0.14).

The correlations between changes in CRP levels and other variables are shown in Table 5. Only changes in serum uric acid, AST, ALT, γ-GTP, and SAA were significantly correlated with CRP changes by Spearman rank correlation. A multiple regression analysis was performed to evaluate the relation of the changes in all studied variables to CRP levels. Changes in SAA and WBC were independently related to changes in CRP (R²=0.23, P<0.0001, P=0.02, for SAA, WBC, respectively).

**Discussion**

After the exercise training program, body weight was significantly reduced and the CRP levels were also significantly lowered. It has been demonstrated that obesity is related to CRP levels, and that adipose tissue is likely a factor modulating CRP levels. We also found strong correlations between BMI, waist girth, and the CRP levels. Therefore, our result is reasonable. However, inconsistent with findings for other conventional risk factors, decreases in CRP levels were not proportionally associated with the extent of weight reduction (Table 4). In the quartile analysis in group D (the largest weight reduction quartile), variables that must be important contributors for CRP, especially triglycerides and insulin resistance, were drastically improved; neverthe-
TABLE 3. Physical and Metabolic Characteristics Before and After Exercise Training in Premenopausal and Postmenopausal Women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before Training</th>
<th>In Premenopausal Women</th>
<th>After Training</th>
<th>Premenopausal Women</th>
<th>Postmenopausal Women</th>
<th>After Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>65.8 (8.3)</td>
<td>62.8 (8.2)§</td>
<td>67.0 (9.1)</td>
<td>63.9 (8.9)§</td>
<td>64.9 (7.6)</td>
<td>62.0 (7.5)§</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>27.3 (3.1)</td>
<td>26.1 (3.0)§</td>
<td>27.3 (3.3)</td>
<td>26.0 (3.2)§</td>
<td>27.4 (2.9)</td>
<td>26.1 (2.9)§</td>
</tr>
<tr>
<td>Abdominal wall fat, mm</td>
<td>32.7 (8.8)</td>
<td>29.2 (9.0)§</td>
<td>32.9 (8.9)</td>
<td>28.9 (9.1)§</td>
<td>32.7 (8.8)</td>
<td>29.5 (8.8)§</td>
</tr>
<tr>
<td>Minimum waist girth, cm</td>
<td>81.5 (7.6)</td>
<td>77.9 (7.5)§</td>
<td>81.4 (7.9)</td>
<td>77.9 (7.7)§</td>
<td>81.9 (7.3)</td>
<td>78.3 (7.4)§</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.83 (0.06)</td>
<td>0.82 (0.06)§</td>
<td>0.82 (0.05)</td>
<td>0.81 (0.05)†</td>
<td>0.84 (0.06)</td>
<td>0.82 (0.06)‡</td>
</tr>
<tr>
<td>Thigh muscle thickness, mm</td>
<td>34.1 (6.1)</td>
<td>34.6 (6.8)</td>
<td>35.2 (6.4)</td>
<td>36.1 (7.1)</td>
<td>33.0 (5.6)</td>
<td>33.0 (6.3)</td>
</tr>
<tr>
<td>Resting heart rate, bpm</td>
<td>77 (11)</td>
<td>72 (10)§</td>
<td>78 (11)</td>
<td>73 (11)§</td>
<td>77 (10)</td>
<td>72 (9)§</td>
</tr>
<tr>
<td>Systolic blood pressure, mm Hg</td>
<td>129 (18)</td>
<td>120 (16)§</td>
<td>127 (18)</td>
<td>118 (16)§</td>
<td>131 (19)</td>
<td>122 (17)§</td>
</tr>
<tr>
<td>Diastolic blood pressure, mm Hg</td>
<td>77 (11)</td>
<td>72 (10)§</td>
<td>78 (11)</td>
<td>73 (10)§</td>
<td>80 (11)</td>
<td>74 (10)§</td>
</tr>
<tr>
<td>White blood cell count, 10^9/L</td>
<td>5.0 (1.1)</td>
<td>4.6 (1.1)§</td>
<td>5.2 (1.0)</td>
<td>4.7 (1.1)§</td>
<td>4.8 (1.2)</td>
<td>4.5 (1.2)‡</td>
</tr>
<tr>
<td>Total cholesterol, mg/dL</td>
<td>223 (31)</td>
<td>204 (27)§</td>
<td>215 (29)</td>
<td>194 (24)§</td>
<td>231 (31)</td>
<td>212 (27)§</td>
</tr>
<tr>
<td>LDL cholesterol, mg/dL</td>
<td>137 (28)</td>
<td>125 (26)§</td>
<td>130 (27)</td>
<td>116 (24)§</td>
<td>144 (27)</td>
<td>132 (26)§</td>
</tr>
<tr>
<td>HDL cholesterol, mg/dL</td>
<td>64 (14)</td>
<td>61 (14)‡</td>
<td>63 (15)</td>
<td>61 (15)</td>
<td>64 (13)</td>
<td>61 (13)‡</td>
</tr>
<tr>
<td>Triglycerides, mg/dL</td>
<td>92 (67–128)</td>
<td>75 (57–107)‡</td>
<td>94 (67–134)</td>
<td>75 (53–106)‡</td>
<td>91 (67–127)</td>
<td>78 (61–111)§</td>
</tr>
<tr>
<td>Total/HDL cholesterol ratio</td>
<td>3.63 (0.86)</td>
<td>3.45 (0.82)§</td>
<td>3.55 (0.85)</td>
<td>3.31 (0.77)§</td>
<td>3.68 (0.83)</td>
<td>3.37 (0.82)§</td>
</tr>
<tr>
<td>Fasting blood sugar, mg/dL</td>
<td>98 (12)</td>
<td>93 (11)§</td>
<td>97 (12)</td>
<td>92 (9)§</td>
<td>99 (12)</td>
<td>94 (21)§</td>
</tr>
<tr>
<td>Fasting insulin, μU/mL</td>
<td>9.1 (6.5–13.2)</td>
<td>7.1 (4.9–10.4)‡</td>
<td>9.5 (7.1–13.2)</td>
<td>7.4 (4.9–9.8)‡</td>
<td>8.6 (5.3–13.1)</td>
<td>7.4 (4.9–9.9)§</td>
</tr>
<tr>
<td>HOMA-R</td>
<td>2.2 (1.5–3.3)</td>
<td>1.6 (1.0–2.5)‡</td>
<td>2.2 (1.6–3.2)</td>
<td>1.6 (1.0–2.4)‡</td>
<td>2.0 (1.2–3.4)</td>
<td>1.6 (1.0–2.4)‡</td>
</tr>
<tr>
<td>Hemoglobin A1c, %</td>
<td>5.2 (0.4)</td>
<td>5.1 (0.4)§</td>
<td>5.1 (0.4)</td>
<td>5.0 (0.4)§</td>
<td>5.3 (0.4)</td>
<td>5.2 (0.4)*</td>
</tr>
<tr>
<td>Uric acid, mg/dL</td>
<td>4.7 (1.0)</td>
<td>4.6 (1.0)†</td>
<td>4.6 (1.0)</td>
<td>4.4 (0.9)*</td>
<td>4.9 (1.0)</td>
<td>4.8 (1.0)</td>
</tr>
<tr>
<td>AST, IU/L</td>
<td>24 (11)</td>
<td>22 (6)§</td>
<td>22 (9)</td>
<td>20 (5)*</td>
<td>26 (12)</td>
<td>22 (6)*</td>
</tr>
<tr>
<td>ALT, IU/L</td>
<td>26 (18)</td>
<td>20 (10)§</td>
<td>24 (18)</td>
<td>19 (9)†</td>
<td>28 (18)</td>
<td>22 (11)§</td>
</tr>
<tr>
<td>γ-GTP, IU/L</td>
<td>35 (25)</td>
<td>23 (19)§</td>
<td>28 (17)</td>
<td>20 (10)§</td>
<td>33 (31)</td>
<td>25 (24)§</td>
</tr>
<tr>
<td>C-reactive protein, mg/L</td>
<td>0.63 (0.28–1.19)</td>
<td>0.41 (0.18–0.80)§</td>
<td>0.54 (0.26–1.02)</td>
<td>0.33 (0.16–0.70)§</td>
<td>0.72 (0.31–1.40)</td>
<td>0.52 (0.22–0.99)§</td>
</tr>
<tr>
<td>Serum amyloid A protein, μg/ml</td>
<td>5.4 (4.4–8.5)</td>
<td>4.1 (3.8–6.7)§</td>
<td>4.6 (2.8–7.0)</td>
<td>3.3 (2.1–5.7)‡</td>
<td>6.2 (3.6–10.5)</td>
<td>4.6 (2.3–8.0)§</td>
</tr>
<tr>
<td>Peak oxygen uptake, l/min per kg</td>
<td>22.1 (3.8)</td>
<td>23.9 (4.3)§</td>
<td>23.4 (3.7)</td>
<td>25.2 (4.1)§</td>
<td>20.9 (3.6)</td>
<td>22.8 (4.1)§</td>
</tr>
<tr>
<td>Exercise time, sec</td>
<td>477 (129)</td>
<td>524 (111)†</td>
<td>564 (147)</td>
<td>571 (103)†</td>
<td>456 (102)</td>
<td>484 (102)†</td>
</tr>
<tr>
<td>Thigh strength, W/kg</td>
<td>11.8 (3.3)</td>
<td>13.1 (3.2)§</td>
<td>12.6 (3.5)</td>
<td>13.8 (3.3)§</td>
<td>11.1 (3.0)</td>
<td>12.4 (3.0)§</td>
</tr>
</tbody>
</table>

Variables are presented as mean (SD), or as median (interquartile range) for skewed variables. LDL denotes low-density lipoprotein; HDL, high-density lipoprotein; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γ-GTP, γ-glutamyl transpeptidase.

*P < 0.05.
†P < 0.01.
‡P < 0.001.
§P < 0.0001, before vs after exercise training.

less, CRP levels were not significantly improved (Figure). The high pace of weight reduction did not necessarily reduce CRP levels. There might be some strong adverse effects that cancelled improvement in CRP levels during high paced weight reduction with exercise. For instance, it has been reported that strenuous exercise can lead to muscle damage and thereby increase inflammation. In addition, important adverse effects of exercise training related to overtraining associated with oxidative stress and free-radical formation have been indicated and might act as an inflammatory stimulus. Likewise, some studies reported that acute strenuous exercise could raise CRP levels. Although we did not evaluate the relation between the extent of weight loss and the intensity of exercise training, the inflammatory stimuli derived from a strenuous exercise might be responsible for the results. The rather increased levels of serum uric acid in group D might possibly be caused by vigorous exercise training. Alternatively, exercise training with an inappropriately low calorie diet could induce a catabolic metabolism and also mediate an overproduction of uric acid, leading to an inflammatory status. These findings suggest that there might be an optimal pace of exercise training with weight loss.

Previously, a few studies examined the effects of diet-induced weight reduction on CRP levels. Bastard et al reported that IL-6, but not CRP, was reduced by weight loss after a very low–calorie diet had been imposed for 3 weeks in 8 lean and 21 obese women, although a trend toward reduced
CRP was noted. On the other hand, Heilbronn et al. found that CRP was significantly decreased by 26% in 83 obese women after weight loss on very low-fat diets for 3 months. Tchernof et al. also reported that weight loss with low-calorie diets for long periods (average, 13.9 months) reduced CRP levels in 26 obese postmenopausal women. In the present study, we used a weight reduction program using exercise training with a simple nutritional education, a program that could also reduce CRP levels. This program is an appropriate and reasonable method for weight reduction in a clinical situation and sustains muscle mass and physical ability. Concerning exercise training, Smith et al. reported that a long-term (6 months) exercise tended to reduce CRP levels in 34 persons at risk of developing ischemic heart disease, but this reduction did not reach statistical significance ($P>0.05$). Although there were differences in the subject's characteristics, the training program, and the length of the training period, it seemed that the small number of

### TABLE 4. Spearman Rank Correlation Coefficients Between Weight Reduction (%), Waist Reduction (%), and Changes in Variables After Exercise Training in 199 Women

<table>
<thead>
<tr>
<th>Variable</th>
<th>Weight Reduction (%)</th>
<th>Waist Reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minimum waist girth</td>
<td>0.48§</td>
<td>NA</td>
</tr>
<tr>
<td>Abdominal wall fat</td>
<td>0.18†</td>
<td>0.12</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.16§</td>
<td>0.63§</td>
</tr>
<tr>
<td>Peak oxygen uptake</td>
<td>0.20*</td>
<td>0.13</td>
</tr>
<tr>
<td>Thigh strength</td>
<td>0.19†</td>
<td>0.03</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.23‡</td>
<td>0.09</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.13*</td>
<td>0.04</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>0.20†</td>
<td>0.14*</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>0.25§</td>
<td>0.01</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.20†</td>
<td>-0.12</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.26‡</td>
<td>0.12</td>
</tr>
<tr>
<td>Fasting blood sugar</td>
<td>0.20†</td>
<td>0.13</td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>0.27§</td>
<td>0.07</td>
</tr>
<tr>
<td>HOMA-R</td>
<td>0.28§</td>
<td>0.07</td>
</tr>
<tr>
<td>Uric acid</td>
<td>-0.11</td>
<td>-0.05</td>
</tr>
<tr>
<td>Serum amyloid A protein</td>
<td>0.12</td>
<td>0.06</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>0.03</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Values are shown as Spearman rank correlation coefficients. LDL denotes low-density lipoprotein; NS, not significant.

* $P<0.05$.
† $P<0.01$.
‡ $P<0.001$.
§ $P<0.0001$.

### TABLE 5. Spearman Rank Correlation Coefficients Between Changes in CRP Levels and Changes in Other Variables After Exercise Training in 199 Women

<table>
<thead>
<tr>
<th>Changes in Variables</th>
<th>Changes in CRP</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>0.08</td>
<td>0.23</td>
</tr>
<tr>
<td>Abdominal wall fat</td>
<td>-0.04</td>
<td>0.49</td>
</tr>
<tr>
<td>Waist-hip ratio</td>
<td>0.05</td>
<td>0.49</td>
</tr>
<tr>
<td>Peak oxygen uptake</td>
<td>0.04</td>
<td>0.51</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.06</td>
<td>0.39</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>0.02</td>
<td>0.74</td>
</tr>
<tr>
<td>TC/HDL ratio</td>
<td>0.01</td>
<td>0.80</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>0.008</td>
<td>0.90</td>
</tr>
<tr>
<td>Fasting insulin</td>
<td>0.06</td>
<td>0.38</td>
</tr>
<tr>
<td>HOMA-R</td>
<td>0.07</td>
<td>0.31</td>
</tr>
<tr>
<td>Uric acid</td>
<td>0.16</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>White blood cell count</td>
<td>0.13</td>
<td>0.06</td>
</tr>
<tr>
<td>Serum amyloid A protein</td>
<td>0.36</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>AST</td>
<td>0.17</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>ALT</td>
<td>0.18</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>γ-GTP</td>
<td>0.16</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

Values are shown as Spearman rank correlation coefficients. LDL denotes low-density lipoprotein.

Changes in representative traditional variables (diastolic pressure, triglycerides, and fasting insulin), CRP, SAA, and serum uric acid after exercise training according to the quartiles of weight reduction. Asterisks indicate a significant difference in changes between before and after exercise training. NS, not significant. * $P<0.05$, † $P<0.01$, ‡ $P<0.001$, § $P<0.0001$. 

![Graphs showing changes in CRP, systolic blood pressure, and diastolic blood pressure after exercise training.](http://atvb.ahajournals.org/forbidden/)
subjects in their study might be a major reason for different statistical results between their study and ours. Besides, there might possibly have been some adverse effects of exercise on CRP in their study setting.

There could be several mechanisms whereby exercise training or weight reduction decrease CRP levels. It has been proposed that adipose tissue–secreted IL-6 and tumor necrosis factor-α may contribute to the elevated CRP levels observed in obesity. Thus, exercise training may reduce CRP levels adequately by reducing adiposity. In addition, increased antioxidant capacity and improved endothelial function by exercise training are potential mechanisms for decreased CRP levels. Improvements in other atherogenic risks as well as weight reduction by exercise training may also be responsible for decreased CRP levels.

In the cross-sectional analysis, in addition to measures of obesity, fasting glucose, insulin, HOMA-R, HbA1c, lipid profiles, and fitness status (exercise tolerance and muscle strength) were significantly correlated to CRP levels. Those variables were significantly improved after the program. Although no significant correlation was observed between changes in CRP and those variables, improvements in those factors likely affected the CRP levels. On the other hand, changes in serum uric acid and other inflammatory variables were significantly correlated with CRP changes. WBC and SAA might be partly coregulated inflammatory variables were significantly correlated with the other hand, changes in serum uric acid and other atherogenic risks as well as weight reduction by exercise training may also be responsible for decreased CRP levels.

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Other important findings of our study were that liver function profiles AST, ALT, and γ-GTP were cross-sectionally and dynamically related to CRP levels. In healthy subjects, the levels of AST, ALT, and γ-GTP might be related to liver fatness. Fatty liver associated with obesity may be the major cause of the relationship between them. Acute phase proteins are produced by the liver through stimulation by inflammatory cytokines, which could be excreted from adipose tissue. It appears that adipose tissue in the liver could stimulate the liver very effectively to produce CRP and SAA.

We observed the subjects for 2 months in the present study. Further study is needed to examine long-term outcomes, and CRP must be measured during maintenance period of target weight.

We conventionally measured the waist girth at the narrowest circumference. It may be difficult to evaluate a precise change in visceral obesity after weight loss with this technique. The precise measurement of a change in visceral obesity could help stimulate further investigation into the factors affecting the changes in CRP levels.

Conclusion

In the present study, we investigated the effect of exercise training with weight reduction on CRP levels in apparently healthy Japanese women. After the training program, all conventional variables of cardiovascular risk were improved, and CRP levels were also significantly lowered. However, in contrast to conventional variables, the changes in CRP were not proportionally associated with the extent of weight reduction. Intensive weight reduction did not necessarily reduce CRP levels but rather raised uric acid levels. Considering inflammatory status, there might be an optimal pace of exercise training and weight reduction.

References

Can Exercise Training With Weight Loss Lower Serum C-Reactive Protein Levels?
Koichi Okita, Hirotaka Nishijima, Takeshi Murakami, Tatsuya Nagai, Noriteru Morita, Kazuya Yonezawa, Kenji Iizuka, Hideaki Kawaguchi and Akira Kitabatake

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