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Effects of aerobic exercise on C-reactive protein, body composition, and maximum oxygen consumption in adults: a meta-analysis of randomized controlled trials

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Abstract

The aim of the study was to use the meta-analytic approach to examine the effects of aerobic exercise on C-reactive protein (CRP) in adults. Secondary outcomes included changes in body weight in kilograms, percentage of body fat, and maximum oxygen consumption ($\dot{V}O_2$max) in mL kg^{-1} min^{-1}. Studies were retrieved using computerized literature searches, cross-referencing, and hand searching. Inclusion criteria were assessment of CRP in randomized controlled trials published in the English language between January 1, 1990, and January 1, 2006. Studies were also limited to aerobic exercise interventions lasting 4 weeks or more in adults 18 years or older. Five studies representing 323 male and female subjects (171 exercise, 152 control) and 6 outcomes for CRP were available for pooling. A nonsignificant reduction of approximately 3% was observed for CRP in the exercise groups (mean ± SEM, −0.11 ± 0.14 mg/L; 95% confidence interval [CI], −0.39 to 0.17 mg/L) using a random-effects model. Statistically significant reductions of approximately 4% were found for body weight (mean ± SEM, −3.4 ± 1.0 kg; 95% CI, −5.3 to −1.5 kg) and percentage of body fat (mean ± SEM, −1.4% ± 0.4%; 95% CI, −2.3% to −0.6%), whereas a statistically significant increase of 12% was found for $\dot{V}O_2$max (mean ± SEM, 3.3 ± 0.9 mL kg^{-1} min^{-1}; 95% CI, 1.5 to 5.1 mL kg^{-1} min^{-1}). The results of our study suggest that aerobic exercise does not reduce CRP levels in adults, but does improve measures of body composition and physical fitness.

1. Introduction

Cardiovascular disease (CVD) is the leading cause of mortality in the United States, affecting a total of 696 947 people (28.5% of all deaths) in 2002 [1]. Current research suggests that inflammation plays an important role in the development of atherosclerosis [2,3]. One of the most important markers of inflammation and subsequent CVD appears to be elevated levels of high-sensitivity C-reactive protein (CRP) [4]. To support this contention, it has been shown that CRP is a better predictor of CVD when compared to lipoprotein(a), homocysteine, interleukin 6, total cholesterol, low-density lipoprotein cholesterol, serum amyloid A, apolipoprotein B, and the ratio of total cholesterol to high-density lipoprotein cholesterol [4]. Given the apparent importance of CRP in the development of CVD morbidity and mortality, it is important to determine those factors that may help to lower and maintain optimal levels of CRP.

One possible approach for improving levels of CRP may be aerobic exercise, a low-cost, nonpharmacologic intervention that is available to most of the general public. For example, a recent qualitative systematic review that examined studies dealing with physical activity and CRP concluded that habitual physical activity results in lower levels of CRP [5]. However, these conclusions were based primarily on the results from observational studies and no randomized controlled trial(s) in which aerobic exercise was the only intervention [5].

Although observational studies can provide important information, they have several potential weaknesses, most notably, selection bias and reporting bias. In contrast, randomized controlled trials are the only way to control

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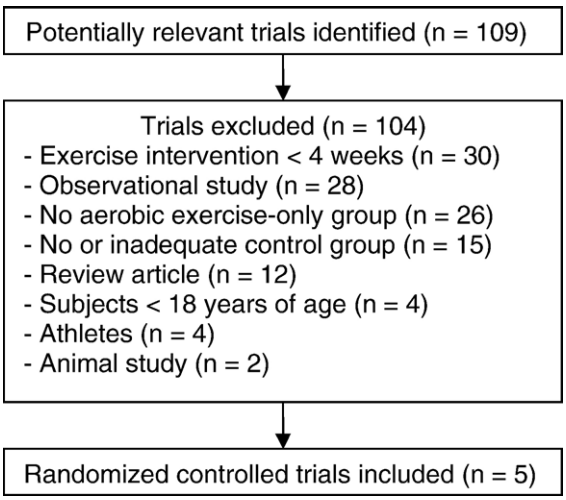

Fig. 1. Flow diagram for the selection of studies. Note that the number of trials excluded exceeds the number of trials actually excluded because some trials were excluded for more than one reason.

for confounders that are not known or measured [6,7]. However, we are not aware of any qualitative or quantitative (meta-analysis) systematic review that has examined the effects of aerobic exercise on CRP while limiting their analysis to randomized controlled trials only.

Meta-analysis is a quantitative approach in which individual studies are combined to arrive at some general conclusions regarding a body of research. The strengths of meta-analysis include the ability to increase estimates of treatment effectiveness as well as statistical power for primary outcomes and other end points [8]. Therefore, given (1) the importance of CRP as a CVD risk factor, (2) the potential for aerobic exercise to lower and maintain levels of CRP, and (3) the strength of randomized controlled trials and the meta-analytic approach, the primary purpose of this study was to use the meta-analytic approach to examine the effects of aerobic exercise on CRP in adult humans while limiting studies to randomized controlled trials. In addition, because aerobic exercise affects many other variables associated with a reduction in the risk for CVD, we also examined its effects on body weight, percentage of body fat, and maximum oxygen consumption ($\dot{V}O_2$max, mL kg^{-1} min^{-1}).

2. Methods

2.1. Data sources

Studies for this meta-analysis were retrieved via computerized literature searches (PubMed, The Cochrane Central Register of Controlled Trials, Sport Discus, Dissertation Abstracts International), cross-referencing from review articles and retrieved studies, and hand searching selected journals. Keywords used in our search included "exercise," "C-reactive protein," "adults," "clinical trial," "humans," and "English." We did not include the keyword "randomized controlled trial" because we felt that we might miss 1 or more studies that met our inclusion criteria.

2.2. Study selection

Studies were included in our meta-analysis if they met the following criteria: (1) randomized controlled trials, (2) long-term aerobic exercise of 4 weeks or more as the only intervention, (3) non-exercise control group, (4) English-language studies published between January 1, 1990, and January 1, 2006, (5) studies published in journals or as dissertations or Master's theses, (6) human subjects 18 years or older, and (7) assessment of CRP. We did not include foreign-language articles because of our concern about the translation and interpretation of findings as well as the lack of financial resources for the translation of such. In addition, we excluded any studies that included a different intervention before the initiation or continuation of a study that met our inclusion criteria. All studies were selected by both authors, independent of each other. They then reviewed their selections for accuracy and precision. Disagreements were resolved by consensus.

2.3. Data abstraction

A coding sheet was developed that could hold up to 229 items from each study. The major categories that were coded included (1) study characteristics (eg, year and source), (2) subject characteristics (eg, age and sex), (3) CRP assessment procedures (eg, time after exercise and instrumentation), (4) training program characteristics (eg, frequency and duration), and (5) primary (changes in CRP expressed in milligrams per liter) and secondary (changes in body weight, percentage of body fat, and $\dot{V}O_2$max) outcomes. All studies were coded by both authors, independent of each other. Both authors then reviewed every entry for accuracy and precision. Discrepancies were resolved by consensus. Interrater agreement before correcting discrepant items was 0.86 using Cohen's [9] κ coefficient.

2.4. Statistical analysis

2.4.1. Primary and secondary outcomes

The primary outcome in our meta-analysis was changes in CRP, expressed in milligrams per liter. However, before conducting any statistical analysis for this review, we conducted power analysis using approaches designed specifically for meta-analysis [10,11]. Unlike traditional studies where power is determined and the appropriate numbers of subjects are then recruited, power analysis prior to conducting any statistical analysis can be determined post hoc since one is limited to the studies and outcomes that meet one's inclusion criteria. Therefore, we conducted power analysis with the following factors included in the calculation: (1) a small to medium effect size of 0.35, (2) a random-effects variance component of 0.33, (3) the number of CRP outcomes available for pooling (6), and (4) the average number of exercise (29) and control (30) subjects

Table 1
Characteristics of randomized controlled trials included

Reference	Subjects	Exercise intervention	CRP assessment
Baslund et al [17]	Eighteen patients (16 females, 2 males) with rheumatoid arthritis assigned to either an exercise (8 females, 1 male) or control (8 females, 1 male) group; age (mean ± SD) of the exercise and control groups were 49 ± 3 and 47 ± 9 y, respectively	Eight weeks of supervised cycle ergometry performed 4-5 times per week for 30 min per session	Single radial immunodiffusion; blood samples collected in the morning after fasting for 8 h and avoiding exercise for at least 36 h
Fairey et al [18]	Fifty-three female, postmenopausal breast cancer survivors assigned to either an exercise (n = 25) or control (n = 28) group; age (mean ± SD) of the exercise and control groups were 59 ± 5 and 58 ± 6 y, respectively	Fifteen weeks of supervised cycle ergometry performed 3 times per week for 15-35 min at 70%-75% of peak oxygen consumption	Enzyme-linked immunosorbent assay; blood samples collected in the morning after fasting for 12 h and avoiding exercise for at least 48 h; duplicate measures made for each blood sample with the mean used as the sample value
Hammett et al [21]	Sixty-one healthy elderly subjects (27 males, 34 females) assigned to an exercise (n = 30) or control (n = 31) group; age (mean ± SD) of the exercise and control groups were 67 ± 5 and 66 ± 4 y, respectively	Twenty-four weeks of aerobic exercise that included 3 supervised and 1 unsupervised session per week for 45 min per session at 80% of VO_2max	Single-batch high-sensitivity assay; blood samples collected 24 h after the last exercise session
Marcell et al [22]	Fifty-one white, overweight, men (n = 20) and women (n = 31) assigned to either moderate-intensity exercise (n = 17), higher-intensity exercise (n = 20) or a control group (n = 14); age (mean ± SD) of the subjects were 47 ± 9 (moderate-intensity group), 44 ± 7 (higher intensity-exercise group), and 44 ± 10 y (control group)	Sixteen weeks of either moderate (no target heart rates set) or higher intensity (80%-90% of age predicted maximum heart rate) walking or jogging performed 5 d/wk for 30 min per session with at least 1 supervised session per week	Immunometric assay (DPC Immulite Diamond Diagnostics, Holliston, MA)
Rauramaa et al [23]	One hundred forty middle-aged men assigned to either an exercise regimen (n = 70) or control (n = 70) group; age (mean ± SD) of the exercise and control groups were both 57 ± 3 y	Six-year study in which subjects were prescribed unsupervised aerobic exercise(s) of their choice (walking, jogging, cross-country skiing, swimming, cycling, etc), 3-5 times per week for 45-60 min per session at 40%-60% of maximal oxygen uptake	Commercial immunoassay (Immulite 2000, Diamond Diagnostics); blood sampling took place after fasting

included in each group from the included studies. Using a 2-tailed α level of .05, the power to detect a statistically significant difference in CRP was 81%.

For each study included in our analysis we calculated changes in CRP by subtracting the change outcome difference in the control group from the change outcome difference in the exercise group. In addition, each study was weighted by the inverse of the variance for that study. Results were then pooled using a random-effects model that controls statistically for heterogeneity as well as providing for wider confidence intervals (CIs) than the fixed-effects model when significant heterogeneity is present [12]. Ninety-five percent

Table 2
Initial characteristics of subjects

Variable	Exercise			Control		
	n[a]	Mean ± SD	Range	n	Mean ± SD	Range
Age (y)	6	54.0 ± 8.6	44-67	5	54.5 ± 8.9	44-66
Body weight (kg)	4	82.9 ± 15	64-98	3	81.6 ± 19.7	63-102
Body fat (%)	3	37.5 ± 3.9	33-40	2	38.4 ± 7.6	33-44
VO_2max (mL kg^{-1} min^{-1})	6	27.4 ± 4.8	19-31	5	25.7 ± 5.5	19-31
CRP (mg/L)	6	3.7 ± 1.7	2-5	5	5.4 ± 5.0	2-14

[a] Number of groups reporting data.

Table 3
Training program characteristics

Variable	n[a]	Mean ± SD	Range
Length (wk)	6	65.2. ± 121	8-312
Frequency (times per week)	6	4.0 ± 1.0	3-5
Intensity (%VO_2max)	5	73.5 ± 13.9	50-85
Duration (minutes per session)	6	34.2 ± 8.6	25-45
Compliance (%)	4	88.4 ± 13.3	71-99

"Compliance" indicates percentage of exercise sessions attended.
[a] Number of groups reporting data.

confidence intervals were used to establish the statistical significance of our results. If the results did not cross zero, they were considered to be statistically significant.

Although a random-effects model controls for statistical, but not clinical, heterogeneity, we also examined for heterogeneity using the Q statistic, a statistic that is based on the fixed-effects model [13]. An α level of .10 was used to determine the statistical significance of the Q statistic. We used an α level of .10 vs .05 because the Q statistic tends to suffer from low power [14].

Secondary outcomes, that is, changes in body weight, percentage of body fat, and $\dot{V}O_2$max (mL kg^{-1} min^{-1}) were analyzed using the same approach as changes in CRP.

To examine the sensitivity of changes in CRP to potential publication bias, that is, the tendency for authors to submit and/or editors to publish studies that yield statistically significant results [15], we used the regression approach of Egger et al [16]. An α level of less than .05 was used to determine if statistically significant publication bias might be present.

Changes in CRP were also examined with each study deleted from the model once. In addition, we analyzed our CRP results with the 2 studies that included subjects in which inflammatory status could have been altered, that is, subjects with osteoarthritis or breast cancer, deleted from the model [17,18]. Furthermore, we performed cumulative meta-analysis, ranked by year, to examine the stability of our results over time [19].

Study quality was assessed using a previously developed 5-point scale that has been shown to be both valid and reliable [20]. The scale ranges from a low of 0 to a high of 5 with higher numbers representing greater study quality.

We did not perform any subgroup comparisons or meta-regression analyses for changes in CRP because of the small number of studies included as well as the lack of statistically significant heterogeneity observed for our pooled results. Descriptive data are reported as mean ± SD, whereas changes in primary and secondary outcomes are reported as mean ± SEM.

3. Results

3.1. Study characteristics

Of the 109 studies reviewed, 5 met our criteria for inclusion [17,18,21-23]. A description of the literature search process, including reasons for those studies excluded, is shown in Fig. 1, whereas a general description of the included studies is shown in Table 1. One study each was conducted in the United States [22], Canada [18], Denmark [17], Finland [23], or New Zealand [21]. Three studies appeared to use an analysis-by-protocol approach to analyze their data [17,18,22], whereas the other 2 used an intention-to-treat approach [21,23].

A total of 11 groups (6 exercise, 5 control) representing 323 male and female subjects (171 exercise, 152 control) and 6 outcomes for CRP were available for pooling. Percentage of dropout for the 2 studies that reported such information [18,23] ranged from 4% to 13% in the exercise groups (mean ± SD, 8.5% ± 6.1%) and 0% to 16% in the control groups (mean ± SD, 7.9% ± 11.1%). Median study quality was 2 of a possible high of 5 (range, 1-5).

3.2. Subject characteristics

Baseline characteristics of the subjects are shown in Table 2. One study was limited to males [23], whereas another was limited to females [18]. The remaining 3 included both males and females [17,21,22]. One study reported that all subjects were postmenopausal [18]. For race/ethnicity, 2 studies reported that all subjects were white [22,23]. For cigarette smoking, one study reported that none of the subjects smoked [18], whereas 2 others reported that some of the subjects smoked [21,23]. None of the studies reported adequate information on the alcohol consumption of the subjects.

Two studies reported that there were no changes in diet during the study [18,23], whereas one study reported that all subjects were sedentary before taking part in the study [22]. All of the studies appeared to have one or more subjects that were taking some type of medication [17,18,21-23].

For comorbidities, 3 studies reported that none of the subjects had any type of diabetes [18,21,22], whereas one reported that some subjects had diabetes [23]. Three studies reported that none of the subjects had CVD at the start of the study [17,18,21], whereas one reported that some of the subjects had CVD [23]. For overweight/obesity, one

Table 4
Primary and secondary outcomes

Variable	n[a]	Mean ± SEM	95% CI	Q (P)
CRP (mg/L)	6	−0.11 ± 0.14	−0.39 to 0.17	8.2 (.15)
Body weight (kg)	3	−3.4 ± 1.0	−5.3 to −1.5	2.8 (.25)
Body fat (%)	3	−1.4 ± 0.4	−2.3 to −0.6	1.7 (.43)
VO_2max (mL kg^{-1} min^{-1})	5	3.3 ± 0.9	1.5 to 5.1	6.4 (.17)

[a] Number of groups reporting data in which a treatment effect could be calculated.

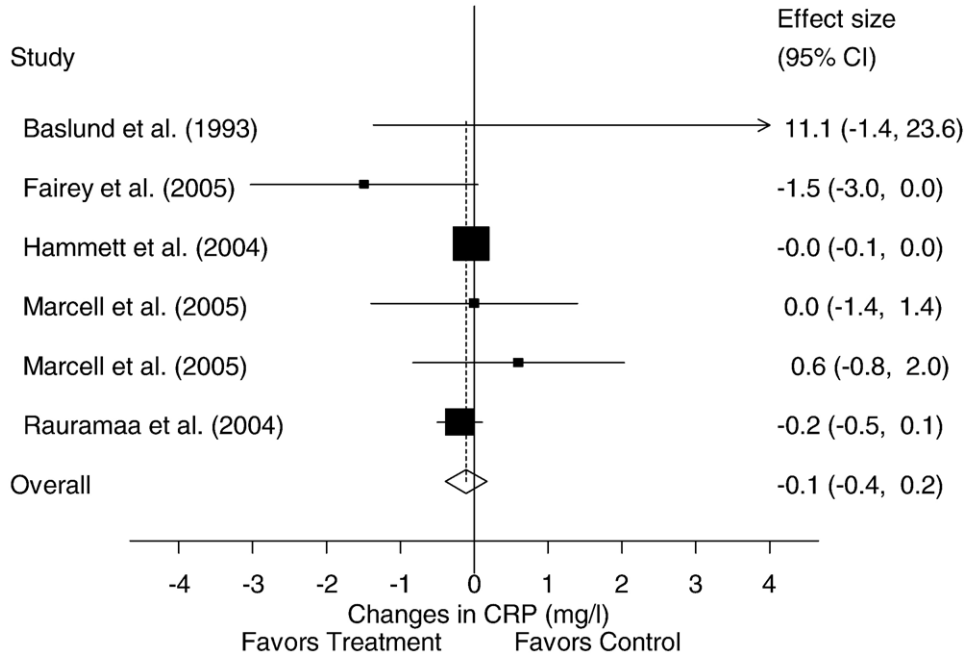

Fig. 2. Forest plot for changes in CRP and 95% CIs for each outcome from each study. The square (weighted) represents the mean change, whereas the left and right extremes of the square represent the lower and upper 95% CIs for each outcome. The overall mean difference for all studies combined is shown by the middle of the diamond, whereas the left and right extremes of the diamond represent the lower and upper 95% CI.

study reported that all subjects were overweight [22], whereas another reported that some subjects were overweight [23]. One study reported that all subjects had breast cancer [18].

3.3. C-reactive protein assessment

A description of the assessment of CRP for each study is shown in Table 1. Three of the studies reported that blood sampling took place in the morning after an overnight fast of between 8 and 12 hours [17,18,23]. Four studies reported that exercise was avoided for 24 to 48 hours before blood sampling [17,18,21,22].

3.4. Training program characteristics

A description of the training program characteristics for each study is shown in Table 1, whereas summary data are provided in Table 3. As can be seen, there was a wide variation in the length of training (8-312 weeks). For training modality, 2 studies reported that subjects participated in cycle ergometry [17,18], 1 reported participation in walking and jogging [22], and another reported participation in a variety of activities, including, but not limited to, walking, jogging, cycling, and swimming. Total minutes of training ranged from 1080 to 56 160 minutes (mean ± SD, 11 167 ± 22 073 minutes). The wide variation in total minutes of training was primarily the result of the wide variation in the length of training. Two of the studies reported that the exercise sessions were supervised [17,18], 1 reported that they were unsupervised [23], whereas the remaining 2 reported a combination of both supervised and unsupervised exercise [21,22].

3.5. Primary and secondary outcomes

A description of overall changes in our primary outcome (CRP) is shown in Table 4, whereas changes for each study are shown in Fig. 2. Although changes in CRP were in the direction of benefit, they were not statistically significant. The observed changes in CRP were equivalent to a relative reduction of approximately 3%. As can be seen, no statistically significant heterogeneity was observed. In addition, and as would be expected, no publication bias was observed ($P = .95$).

Results for CRP with each study deleted from the model once can be found in Table 5. As shown, results remained statistically nonsignificant with each study deleted from the model once. In addition, no statistically significant differences were observed when we analyzed our CRP results with the 2 studies that included subjects in which inflammatory status could have been altered deleted from the model (mean ± SEM, −0.05 ± 0.12 mg/L; 95% CI, −0.12 to 0.03 mg/L) [17,18]. Cumulative meta-analysis, ranked by year, also demonstrated that results have remained statistically nonsignificant since the time of the first study on this topic.

Table 5
Changes in CRP with each study deleted once

Study omitted	Mean ± SEM	95% CI
Baslund et al [17]	−0.09 ± 0.10	−0.28 to 0.10
Fairey et al [18]	−0.06 ± 0.09	−0.24 to 0.11
Hammett et al [21]	−0.19 ± 0.39	−0.95 to 0.58
Marcell et al [22]	−0.16 ± 0.18	−0.50 to 0.18
Rauramaa et al [23]	−0.11 ± 0.38	−0.86 to 0.63

Overall changes in secondary outcomes are shown in Table 4. As can be seen, statistically significant improvements were found for body weight, percentage of body fat, and $\dot{V}O_2$max. These changes were equivalent to a relative reduction of approximately 4% for body weight and percentage of body fat as well as an approximate 12% increase in $\dot{V}O_2$max. No statistically significant heterogeneity was observed for any of these outcomes.

4. Discussion

The purpose of this study was to use the meta-analytic approach to examine the effects of aerobic exercise on CRP in adults 18 years and older. Despite statistically significant improvements in body weight, percentage of body fat, and $\dot{V}O_2$max, changes in CRP as a result of aerobic exercise and across a variety of patient and training program characteristics were not statistically significant. These findings remained true when each study was deleted from the model once as well as when results were examined cumulatively over time. Therefore, the inclusion of studies such as those in which all subjects had rheumatoid arthritis did not change the results of this study [8].

Our findings are consistent with the individual trials themselves as all trials we included yielded nonsignificant findings ($P > .05$ for all) [17,18,21-23]. Given the nonsignificant findings of our included trials, one could question the rationale for conducting a meta-analysis. However, it is not uncommon for meta-analysis to yield a statistically significant finding in situations such as this because of the ability of meta-analysis to increase estimates of treatment effectiveness as well as statistical power for primary outcomes and other end points [8].

The results for CRP from our meta-analysis as well as the individual studies included are in sharp contrast to the findings from a recent qualitative systematic review on this topic that correctly concluded, based on the evidence reviewed, that both observational and interventional studies suggested that exercise training improved CRP levels [5]. One of the reasons for the discrepant findings may have to do with the different types of study designs included. For example, in the review by Kasapis and Thompson [5], cross-sectional studies, which are prone to recall and self-report bias, comprised the bulk of the review. In addition, of the 3 exercise training studies reviewed, one did not include a control group [24], another included a nonrandomized control group [25], whereas still another was a randomized controlled trial in which aerobic exercise was not the only intervention [26]. In contrast, our meta-analysis was limited to randomized controlled trials in which aerobic exercise was the only primary intervention. Given (1) our stricter inclusion criteria, (2) the fact that randomized controlled trials are considered to be the "gold standard" of study designs because they are the only way to control for confounders that are not known or measured, and (3) the observation that nonrandomized controlled trials tend to overestimate the effects of health care [6,7], our results may be more valid in relation to the effects of aerobic exercise on CRP in adults. Alternatively, it may be that one has to be exposed to regular exercise over a longer period than the training protocols included in our studies to experience any CRP-lowering benefits. If this is true, then the results of observational studies that comprised the bulk of the review by Kasapis and Thompson [5] may be more valid. Given the discrepant findings described above, it would appear that a large, long-term, randomized controlled trial on this topic is warranted.

Although the focus of our meta-analysis was on the independent effects of aerobic exercise on CRP, it may be that exercise in combination with other lifestyle interventions may yield the greatest benefit. For example, in a randomized trial conducted by You et al [27], 6 months of diet plus exercise training, but not diet alone, resulted in statistically significant reductions in CRP among obese postmenopausal women. In another study, Esposito et al [28] conducted a randomized controlled trial and found statistically significant reductions in CRP after 2 years of increased physical activity and a Mediterranean-style diet in obese women. Furthermore, Milani et al [29] found statistically significant reductions in CRP as a result of exercise training and diet in both men and women with coronary heart disease. Given these findings, it may be that the greatest reductions in CRP may be derived from a combination of exercise and other lifestyle modifications such as diet.

The fact that we did not find any statistically significant decreases in CRP as a result of aerobic exercise may be related to the inability to isolate those subjects with elevated CRP levels. Currently, values of less than 1.0, 1.0 to 3.0, and more than 3.0 mg/L correspond to the relative risk categories of low, moderate, and high, respectively [2]. Although our overall mean CRP level was 3.7 mg/L with a between-study group range of 2 to 14 mg/L, the isolation of only those subjects with CRP levels of 3.0 mg/L and higher may have yielded different results. To support this possibility, a recent no-control study in sedentary black and white women and men found that 20 weeks of aerobic exercise did not significantly reduce CRP levels for those in the low (< 1.0 mg/L) and moderate (1.0-3.0 mg/L) risk categories, but did significantly reduce CRP levels for those in the high-risk category (>3.0 mg/L) [30]. Although our overall mean CRP levels would place subjects in the category of "high risk," we were unable to stratify our results according to only those subjects in the high-risk category because the summary means meta-analysis approach we used incorporates the mean values from studies vs the individual patient data. Thus, unless the studies themselves limit their inclusion criteria to only those subjects with CRP levels of 3.0 mg/L and higher, a summary means meta-analysis will be unable to isolate those subjects with CRP levels of 3.0 mg/L and above. A potentially better approach to addressing this issue may be to conduct an individual patient data meta-analysis

[31]. However, this must be considered with respect to the increased time and resources for the conduct of such, and more importantly, the difficulty in obtaining individual patient data from study investigators [32].

Although the results of our meta-analysis suggest that aerobic exercise does not lower CRP levels in adults, aerobic exercise, unlike pharmacologic interventions, should almost always be recommended because of the numerous other benefits that can be derived from such. For example, in our study, we found statistically significant and clinically important reductions of approximately 4% in body weight and percentage of body fat. Because overweight and obesity are reaching epidemic proportions in many countries and has been associated with an increased risk for conditions such as myocardial infarction [33], participation in a regular program of aerobic exercise should help to improve and maintain optimal levels of body composition and reduce cardiovascular risk.

One of the most common physiologic adaptations that occur as a result of aerobic exercise is an increase in $\dot{V}O_2$max. The statistically significant increase of approximately 12% that we observed for $\dot{V}O_2$max is clinically important because it has been shown that adults with higher levels of $\dot{V}O_2$max are at a lower risk for all-cause and cardiovascular disease mortality in both men and women [34]. For example, the increase in $\dot{V}O_2$max observed in our study has been shown to reduce the risk of all-cause mortality by 17% in men [35] and 16% in women [36].

Because the studies included in our meta-analysis followed the general guidelines for improving and maintaining cardiorespiratory fitness in adults [37], adherence to such a program should bring about the changes observed in our meta-analysis. Generally, this includes training 3 to 5 d/wk at an intensity of 40% to 85% of maximum oxygen uptake reserve for 20 to 60 minutes of continuous or intermittent (minimum of 10-minute bouts accumulated throughout the day) aerobic activity, for example, walking, jogging, cycling, swimming [37]. Participation in an exercise program such as described above is also associated with a low-risk of musculoskeletal injury [38].

The findings of our study must be viewed with respect to the following potential limitations. First, meta-analysis, like any type of review, is limited by the information available in the studies. For example, it is probably inappropriate to generalize our results beyond the subject and training program characteristics of the studies included in our meta-analysis. In addition, despite the fact that there was no statistically significant heterogeneity for our CRP results, it would have still been important to examine the relationship between such factors as changes in percentage of body fat on changes in CRP levels. However, because of the small number of studies included, we were unable to do so.

A second potential limitation may have to do with the small number of studies included in our meta-analysis. For example, although we demonstrated that we were adequately powered to conduct the proposed analysis, it does not mean that CRP results would not reach statistical significance at some later point in time as more randomized controlled trials on this topic are conducted. Therefore, we view this meta-analysis as a starting point from which future meta-analytic work can be conducted as additional randomized controlled trials are completed.

A third potential limitation has to do with the meta-analytic approach itself. For example, given the mechanical aspects of meta-analysis, it can be difficult to identify some of the more qualitative differences between studies [39]. Consequently, a traditional, narrative review may be the more appropriate approach to use for identifying some of these subtle differences.

In conclusion, the results of our study suggest that aerobic exercise does not lower CRP levels, but does reduce body weight and percentage of body fat as well as increase $\dot{V}O_2$max in adults.

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