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Effects of aerobic exercise on inflammatory factors in healthy adults: a meta-analysis

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Abstract. – OBJECTIVE: With this meta-analysis we aimed at systematically evaluating the intervention effects of aerobic exercise on inflammatory factors in healthy adults and identifying an optimal aerobic exercise program with anti-inflammatory effects.

MATERIALS AND METHODS: Four databases, including PubMed, Web of Science, Cochrane Library and SPORTDiscus, were searched from inception until April 30, 2021. Stata version 11.0 was used for data analysis.

RESULTS: A total of 15 studies with 1160 participants were included. The pooled estimates showed that aerobic exercise could significantly reduce TNFα levels (SMD=-0.30, 95% CI: -0.58 – -0.03, *p*=0.032), while the levels of IL-6 (SMD=-0.14, 95% CI: -0.32-0.03, *p*=0.109) and CRP (SMD=-0.09, 95% CI: -0.34-0.16, *p*=0.484) were not significantly affected.

CONCLUSIONS: Aerobic exercise exerts a positive effect by preventing inflammation-related diseases.

Key Words:
Aerobic exercise, Inflammatory factors, Meta-analysis.

Introduction

Inflammation is well-established to be positively correlated with the prevalence of chronic diseases, estimated to cause 3.2 to 5.3 million deaths per year worldwide (approximately 9% of all-cause mortality) and associated with economic costs for more than $675 billion[1,2]. In humans, systemic inflammatory factors rise steadily from 30 years of age[3] and are more pronounced in sedentary and physically inactive populations[4]. Aerobic exercise is widely recognized as an effective mean for preventing obesity, type 2 diabetes, and non-communicable chronic diseases such as cardiovascular diseases[5,6]. At the same time, aerobic exercise minimizes disturbances to the intracellular environment and allows cells to recover sufficiently to become more stress-resistant, thereby slowing biological aging and fighting inflammation[7,8]. This study aimed at providing a comprehensive understanding of the effect of aerobic exercise on inflammatory factors in healthy adults and identifying an optimal aerobic exercise program to reduce the prevalence of chronic diseases in sedentary populations.

Materials and Methods

Design and Search Strategy

This meta-analysis was conducted in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[9]. Four databases, including PubMed, Web of Science, Cochrane Library and SPORTDiscus were searched from inception until April 30, 2021. The keywords and subject terms were "aerobic exercise", "inflammation", "inflammatory factors", "RCT", "randomized controlled trial", and "healthy volunteers".

Inclusion Criteria

(1) The study was designed as a randomized controlled trial (RCT) that assessed the effects of any aerobic exercise on biomarkers of peripheral inflammation in healthy subjects, with no significant difference between the experimental group and control group before the trial. (2) The subjects were healthy adults with no history of long-term drug intake, cardiovascular disease,

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and obesity. (3) The intervention was any form of aerobic exercise, with no treatment or placebo in the control group. (4) Outcome indicators were inflammatory biomarkers, such as interleukin-6 (IL-6), C-reactive protein (CRP), and tumor necrosis factor-alpha (TNFα).

Exclusion Criteria

(1) People with any medical disorders. (2) The description of the experimental data was not clear, and the differences before and after the experiments could not calculated. (3) The intervention method was non-aerobic exercise. (4) The study was not written in English or published in journals without an impact factor. (5) Conference and review literature.

Data Extraction

All the retrieved literature was imported into the EndNote Bibliographic software to exclude duplications. The screening of the literature was performed by two researchers independently. After screening, the extracted literature was compared by the two researchers, and in case of disagreement, the decision to include the study was discussed jointly with a third researcher. The extracted information included: first author, year of publication, country of study, number of participants, age and sex of participants, BMI of participants, duration, intensity, frequency of aerobic exercise intervention; outcome indicators: plasma or serum inflammatory factors (IL-6, CRP, TNFα).

Quality Evaluation

The methodological quality and risk of bias of each included study were assessed using the Physiotherapy Evidence Database (PEDro) scale[10], with a score ranging from 0 to 10 points. Each satisfied item contributes for one additional point to the total score. The total score of the scale is 10 points. If it meets the standard, 1 point will be added. If it fails to meet the standard, 0 points will be given. The scale is divided into four grades according to the score. 9-10 points were defined as high quality, 6-8 points as good quality, 4-5 points as medium quality, and < 4 points as very poor quality. GRADE (Grading of Recommendation, Assessment, Development and Evaluation) system was used to evaluate the evidence level of each result[11]. The evaluation criteria included: (1) Randomized controlled trials were initially defined as high quality. (2) The quality level was reduced if there was unexplained heterogeneity. (3) The quality level was improved if there was a dose-response relationship.

Statistical Analysis

In this study, a random-effects model was used for the net change in inflammatory biomarker concentrations (change in the intervention group minus change in the control group), and the combined effect sizes were calculated and expressed as standardized mean differences (SMD) with their 95% confidence intervals (95% CI). Sensitivity analysis was used to assess the robustness of the primary meta-analysis results and subgroup analysis to investigate potential sources of heterogeneity. Meta-regression analysis was used to test for differences between groups and to further explore sources of heterogeneity. A p-value < 0.1 was used to determine statistically significant differences during regression analysis. The Cochrane Q test was used to test for heterogeneity between studies[12]. $I^2 < 25\%$ indicated almost no heterogeneity, 25-50% indicated moderate heterogeneity, and > 50% indicated high heterogeneity, with $p < 0.05$ indicating statistical significance. The presence of publication bias was assessed using Begg's test and Egger's test[13], and all analyses were performed using STATA version 11.0 (StataCorp LLC, College Station, TX, USA).

Results

Literature Search

The initial literature search yielded a total of 1876 publications from four databases, and 1,074 duplicates were removed by EndNote software. After eliminating 756 publications by reading the title and abstract, 318 potentially eligible publications were obtained. After reading the full text, studies with non-healthy subjects (n=87), non-RCT trials (n=112) and inconsistent intervention modalities (n=104) were excluded, and 15 randomized controlled trials were finally included for analysis in our study (Figure 1).

Basic Information of Included Literatures

15 articles[7,14-27], published between 2008 and 2020 with a total sample size of 1,160 people, were included in our study. Besides one study[15] that did not provide information on the age, the average age of participants in the remaining studies ranged from 21 to 78.3 years (Table I).

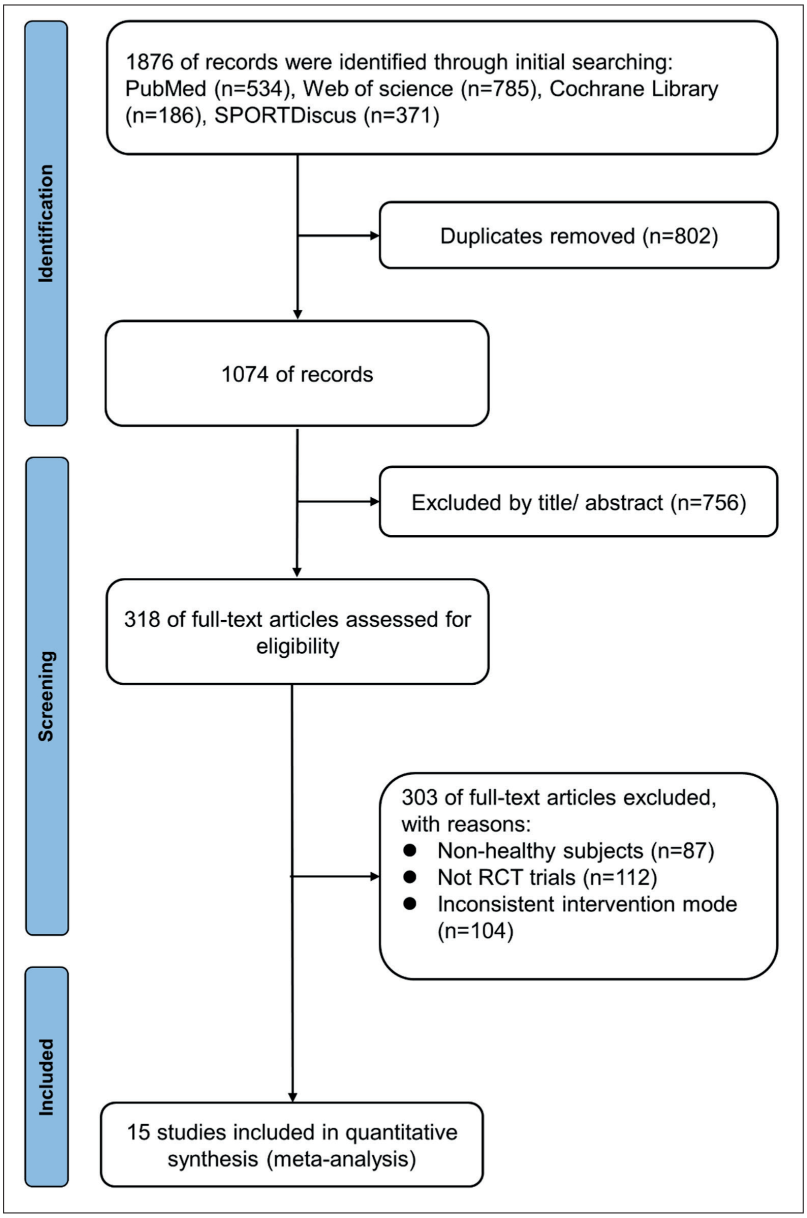

Figure 1. Flowchart of the literature retrieval process.

Result Evidence Level

As shown in Table II, according to the GRADE evidence rating criteria, the evidence level for IL-6 and CRP levels was low due to the absence of significant effects and considerable heterogeneity in the results of the preliminary meta-analysis. This finding indicates that the credibility of the results of the available evidence is not high, and the actual effect may be significantly different from the estimated value. As for TNFα levels, given the presence of significant effects and the absence of considerable heterogeneity, the evidence level was high, indicating that the results are highly reliable, and the effect observed in the study is close to the actual effect.

Meta-Analysis

IL-6 in Healthy Adults

12 studies[7,15-19,21-26], involving a total of 20 intervention groups, reported the effect of aerobic exercise on the level of inflammatory factor IL-6 in healthy adults. The pooled estimates showed that aerobic exercise had no significant effect on IL-6 level (SMD = -0.14, 95% CI: -0.32-0.03, p = 0.109), and there was high heterogeneity (I^2 = 49.8%, p = 0.006), as shown in Figure 2. Sensitivity analysis showed that geographical and gender factors yielded no significant effect on IL-6 levels, while age > 60 years old (SMD = -0.42, 95% CI: -0.79 – -0.04, p = 0.029) could

Table I. Characteristics of included studies in this meta-analysis (15 studies).

Author	Year	Age	Country	Experimental group/ control group (n)	Comparators	Intervention	Duration	Outcome	PEDro score
Alghadir et al[14]	2016	69.7 years	Saudi Arabia	50/50	No description	Exercise mode: stretching and walking (5-10 minutes); Treadmill, bicycle and stair training (45-60 minutes). Strength: 30-45% VO_{2max} Frequency: 3 times/week	24 weeks	CRP	7
Buyukyazi et al[7]	2017	41.4 years	Turkey	22/8	No physical exercise	Exercise mode: preheating (5 minutes); Walk (30-50 minutes); Cool (5 minutes). Intensity: 50-55% HRmax (medium speed walking group)/70-75% HRmax (fast walking group) Frequency: 3 days/week	8 weeks	IL-6	7
Campbell et al[15]	2008	55.4 years	USA	91/97	Maintain daily activity level	Exercise mode: 60 minutes/day Strength: 60-85% HRmax Frequency: 6 days/week	48 weeks	CRP	7
Donges et al[16]	2010	No description	Australia	41/26	Maintain a sedentary lifestyle and diet	Exercise mode: preheating (5 minutes); Cycling (30-50 minutes); Stretch (5 minutes). Strength: 70-75% HRmax Frequency: 2-3 times/week	0 weeks 1	IL-6, CRP	7
Garten et al[17]	2019	24 years	USA	10/10	Keep sitting for 3 hours	Exercise mode: preheating (10 minutes); High intensity intermittent aerobic cycling (28 min) Strength: 85-95% HRmax Frequency: no description	3 hours	IL-6	7
Lee et al[18]	2012	40.1 years	The Republic of Korea	15/7	Maintain previous nutritional patterns	Exercise mode: treadmill running intensity: 50% VO_{2max} or 70% VO_{2max} of maximum oxygen uptake Frequency: 3-5 times/week	14 weeks	IL-6, CRP, TNFα	7
Libardi et al[19]	2012	48.8 years	Brazil	12/13	Maintain daily activities	Exercise mode: walking or running (60 minutes) Strength: 55-85% VO_{2max} Frequency: no description	16 weeks	IL-6, CRP, TNFα	7

Continued

Table I *(Continued)*. Characteristics of included studies in this meta-analysis (15 studies).

Author	Year	Age	Country	Experimental group/ control group (n)	Comparators	Intervention	Duration	Outcome	PEDro score
Lira et al[20]	2017	26.4 years	Brazil	20/10	No physical exercise	Exercise mode: preheating (5 minutes); 5K interval running: running (1 minute) + recovery (1 minute) (high-intensity interval training group)/5K continuous running (steady-state training group) Aerobic training group: n = 10% (steady-state training group, n = 10, maximum intensity training group) Frequency: 3 times/week	5 weeks	IL-6, CRP, TNFα	7
Martins et al[21]	2010	78.3 years	Portugal	18/13	Do not take physical exercise and maintain healthy living habits	Movement mode: preheating; Aerobic exercise; Cooling (45 minutes) Intensity: 40-50% to 71-85% heart rate reserve Frequency: 3 times / week	16 weeks	CRP	7
Masala et al[22]	2020	58.7 years	Italy	57/57	Accept general recommendations on healthy eating and physical activity patterns	Exercise mode: work, cycling, etc. (< 1 hour/day) Strength: medium Frequency: Daily	96 weeks	IL-6, CRP, TNFα	8
Meyer et al[23]	2019	50 years	USA	126/132	Observation control	Exercise mode: cognitive behavior problems (1.5 hours) + warm-up; Aerobic exercise; Cooling (1 hour) + half day rest intensity: medium Frequency: 1 class hour/week	8 weeks, 25 weeks	IL-6, CRP	8
Nishida et al[24]	2015	70.1 years	Japan	31/31	Maintain daily lifestyle	Exercise mode: step exercise (10-20 minutes). Intensity: corresponding to lactate threshold Frequency: 3 times/day	12 weeks	IL-6, CRP, TNFα	8

Continued

Table I ***(Continued).*** Characteristics of included studies in this meta-analysis (15 studies).

Author	Year	Age	Country	Experimental group/ control group (*n*)	Comparators	Intervention	Duration	Outcome	PEDro score
Paolucci et al[25]	2018	21 years	Canada	37/18	Maintain a sedentary lifestyle	Exercise mode: high intensity interval training group: warm-up (3 min); Cycle at 10 high-intensity intervals of 60 seconds and 10 active recovery intervals of 60 seconds (20 minutes); Cool (2 minutes). 40% watts or maximum strength Frequency: 3 times/week	6 weeks	IL-6, CRP, TNFα	7
Ranadive et al[26]	2014	66.5 years	USA	28/27	In the temperature control room (40 minutes)	Exercise mode: moderate intensity aerobic exercise (40 minutes) Strength: 55-65% HRmax Frequency: no description	40 minutes	IL-6, CRP	9
Sloan et al[27]	2018	31 years	USA	45/58	Maintain a sedentary lifestyle	Exercise mode: preheating + cooling (10-15 minutes); Exercise (30-40 minutes). Strength: 55-75% HRmax Frequency: 4 class hours/week	12 weeks	IL-6, CRP, TNFα	8

Abbreviations: CRP, C-reactive protein; IL6, interleukin 6; TNFα, tumor necrosis factor α; HRmax, maximum heart rate; VO_c, maximum oxygen uptake.

Table II. Evaluation of the evidence levels of the results.

	Risk of bias	Atypism	Not direct	Imprecise	Publication bias	Effect quantity	Residual confounding	Dose response	Grade rating
IL-6	0	-1†	0	-1‡	0	0	0	0	Low
CRP	0	-1†	0	-1‡	0	0	0	0	Low
TNFα	0	0	0	0	0	0	0	0	High

Notes: †There is significant and unexplainable heterogeneity in the preliminary meta-analysis; ‡95% confidence interval of effect quantity in preliminary meta-analysis.

significantly reduce the expression of IL-6. Subgroup analysis showed that a BMI of 18.5-25 (SMD = -0.24, 95% CI: - 0.45 – -0.02, p = 0.032), exercise duration < 1 day (SMD = -0.55, 95% CI: - 0.81 – -0.30, p = 0.000) or > 12 weeks (SMD = -0.38, 95% CI: - 0.68 – -0.07, p = 0.015), and moderate exercise intensity (SMD = -0.22, 95% CI: - 0.43 – -0.07, p = 0.109) could significantly reduce IL-6 levels (Table III). Therefore, the heterogeneous effects of aerobic exercise on IL-6 level may be due to age, BMI, exercise duration, and exercise intensity.

CRP in Healthy Adults

10 studies involving 17 intervention groups[14-16,18,19,21-23,25,26] reported the effect of aerobic exercise on the level of inflammatory factor CRP in healthy adults. The meta-analysis showed that aerobic exercise had no significant effects on CRP levels (SMD = -0.09, 95% CI: - 0.34 – 0.16, p = 0.484), and there was high heterogeneity (I^2 = 78.8%, p = 0.000) (Figure 3). As shown in Table III, sensitivity and subgroup analyses showed that region, age, gender, BMI, exercise duration and exercise intensity could not significantly re-

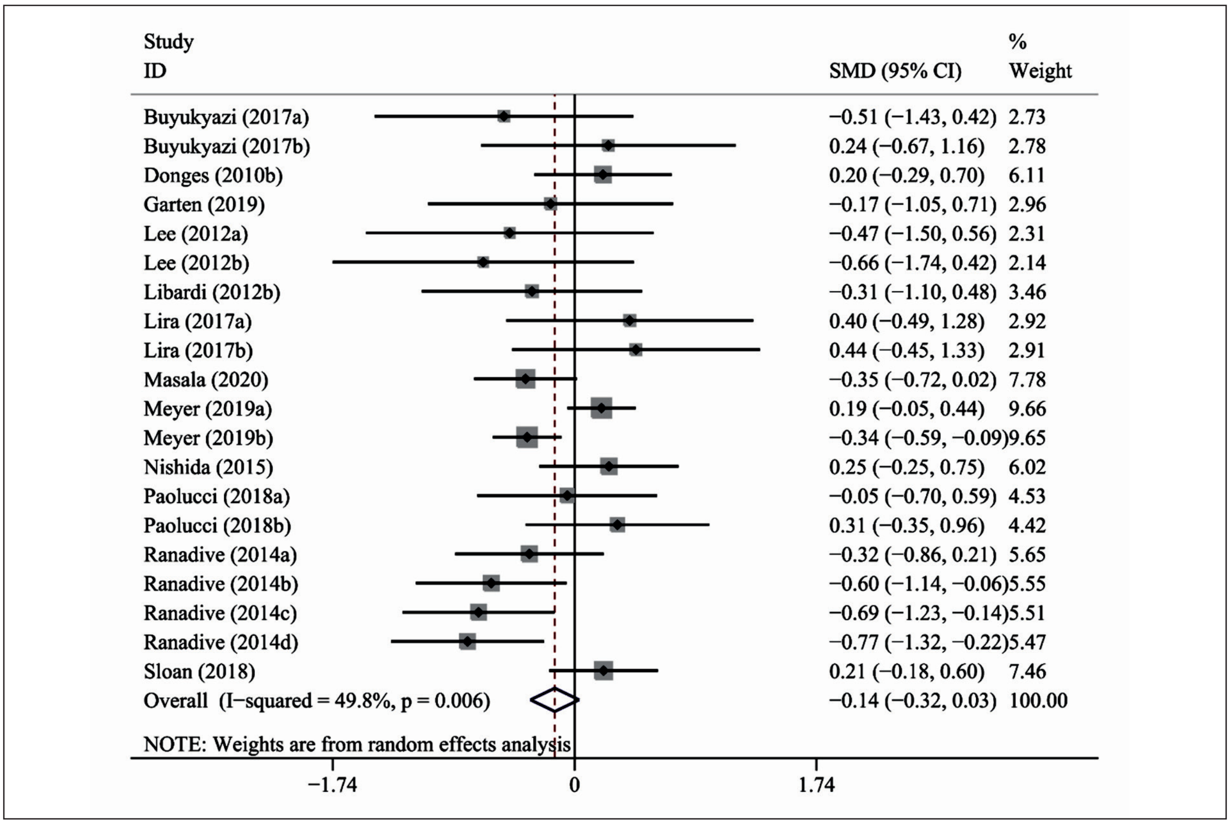

Figure 2. Forest diagram of the effect of aerobic exercise on IL-6 level of healthy adults.

Table III. Results of sensitivity analysis, subgroup analysis and publication bias stratified by study characteristics.

Outcomes	Interventions	SMD (95% CI)	p^1	Heterogeneity test		Regression analysis (p^3)	Publication bias test (p^4)	
				I^2 (%)	p^2		Begg's test	Egger's test
IL-6	-	-	-	-	-	-	-	-
Overall	20	-0.14 (-0.32, 0.03)	0.109	49.8	**0.006**	-	0.417	0.759
Region	-	-	-	-	-	0.724	-	-
Asia	5	-0.07 (-0.46, 0.31)	0.720	11.3	0.342	-	-	-
Europe	1	-0.35 (-0.72, 0.02)	0.061	-	-	-	-	-
America	13	-0.16 (-0.38, 0.07)	0.170	59.9	**0.003**	-	-	-
Oceania	1	-0.20 (-0.29, 0.70)	0.418	-	-	-	-	-
Gender	-	-	-	-	-	0.512	-	-
Male	4	0.06 (-0.36, 0.49)	0.770	0.0	0.503	-	-	-
Female	6	-0.18 (-0.48, 0.12)	0.233	16.3	0.079	-	-	-
Blend	10	-0.17 (-0.42, 0.07)	0.171	68.5	**0.001**	-	-	-
Age	-	-	-	-	-	**0.042**	-	-
< 45 years old	10	0.08 (-0.15, 0.30)	0.507	0.0	0.638	-	-	-
45-60 years old	4	-0.17 (-0.50, 0.16)	0.306	73.0	**0.011**	-	-	-
> 60 years old	5	**-0.42 (-0.79, -0.04)**	**0.029**	59.3	**0.043**	-	-	-
BMI	-	-	-	-	-	**0.096**	-	-
18.5-25	14	**-0.24 (-0.45, -0.02)**	**0.032**	55.8	**0.006**	-	-	-
< 18.5	6	0.06 (-0.23, 0.35)	0.688	28.8	0.219-	-	-	-
Exercise duration	-	-	-	-	-	0.293	-	-
< 1 day	5	**-0.55 (-0.81, -0.30)**	**0.000**	0.0	0.683	-	-	-
1-12 weeks	11	-0.08 (-0.11, 0.28)	0.396	38.0	0.096	-	-	-
> 12 weeks	4	**-0.38 (-0.68, -0.07)**	**0.015**	0.0	0.954	-	-	-
Exercise intensity	-	-	-	-	-	**0.055**	-	-
Low	1	-0.47 (-1.50, 0.56)	0.109	-	-	-	-	-
Medium	14	**-0.22 (-0.43, -0.02)**	**0.033**	58.3	**0.003**	-	-	-
High	5	-0.22 (-0.09, -0.54)	0.162	0.0	0.910	-	-	-

Continued

Table III *(Continued)*. Results of sensitivity analysis, subgroup analysis and publication bias stratified by study characteristics.

				Heterogeneity test			Publication bias test (p^4)	
CRP	Interventions	SMD (95% CI)	p^1	I^2 (%)	p^2	Regression analysis (p^3)	Begg's test	Egger's test
Overall	17	-0.09 (-0.34, 0.16)	0.484	78.8	**0.000**	-	0.434	0.820
Region	-	-	-	-	-	**0.017**	-	-
Asia	3	-0.87 (-2.38, 0.64)	0.035	89.5	**0.000**	-	-	-
Europe	2	0.07 (-0.25, 0.40)	0.212	0.0	0.921	-	-	-
America	11	0.06 (-0.06, 0.18)	0.747	0.0	0.907	-	-	-
Oceania	1	-0.10 (-0.59, 0.39)	0.994	-	-	-	-	-
Gender	-	-	-	-	-	0.592	-	-
Male	2	0.21 (-0.15, 0.57)	0.484	0.0	0.441	-	-	-
Female	4	-0.04 (-0.34, 0.16)	0.784	0.0	0.545	-	-	-
Age	-	-	-	-	-	0.531	-	-
< 45 years old	4	-0.02 (-0.41, 0.37)	0.934	0.0	0.601	-		
45-60 years old	6	0.04 (-0.09, 0.18)	0.532	0.0	0.841	-	-	-
> 60 years old	6	-0.24 (-1.04, 0.55)	0.546	92.2	**0.000**	-	-	-
Exercise duration	-	-	-	-	-	0.224	-	-
< 1 day	4	0.13 (-0.13, 0.16)	0.334	0.0	0.514	-	-	-
1-12 weeks	5	0.02 (-0.14, 0.17)	0.816	0.0	0.986	-	-	-
> 12 weeks	8	-0.28 (-0.88, 0.32)	0.362	89.3	0.000	-	-	-
Exercise intensity	-	-	-	-	-	0.018	-	-
Low	2	-0.93 (-3.23, 1.36)	0.424	93.9	**0.000**	-	-	-
Medium	12	0.04 (-0.09, 0.16)	0.566	0.0	0.936	-	-	-
High	1	-0.12 (-0.41, 0.17)	0.753	80.7	**0.000**	-	-	-
BMI	-	-	-	-	-	0.094	-	-
< 18.5	4	-0.48 (-1.58, 0.61)	0.387	94.4	**0.000**	-	-	-
18.5-25	13	0.05 (-0.07, 0.16)	0.449	0.0	0.858	-	-	-

Continued

Table III *(Continued)*. Results of sensitivity analysis, subgroup analysis and publication bias stratified by study characteristics.

TNFα	Interventions	SMD (95% CI)	p^1	Heterogeneity test		Regression analysis (p^3)	Publication bias test (p^4)	
				I^2 (%)	p^2		Begg's test	Egger's test
Overall	10	**-0.30 (-0.58, -0.03)**	**0.032**	43.9	0.066	-	0.107	0.166
Region	-	-	-	-	-	0.582	-	-
Asia	3	-0.23 (-0.65, 0.18)	0.265	0.0	0.825	-	-	-
Europe	1	-0.09 (-0.46, 0.28)	0.629	-	-	-	-	-
America	6	-0.47 (-0.97, 0.02)	0.060	66.9	**0.010**	-	-	-
Gender	-	-	-	-	-	0.115	-	-
Male	3	**-0.92 (-1.80, -0.04)**	**0.040**	63.5	0.065	-	-	-
Female	4	-0.15 (-0.43, 0.12)	0.271	0.0	0.885	-	-	-
Blend	3	-0.12 (-0.58, 0.28)	0.546	37.2	0.203	-	-	-
Age	-	-	-	-	-	0.859	-	-
< 45 years old	7	-0.36 (-0.80, 0.07)	0.100	57.1	**0.030**	-	-	-
45-60 years old	2	-0.31 (-0.92, 0.29)	0.313	51.6	0.151	-	-	-
> 60 years old	1	-0.24 (-0.74, 0.26)	0.344	-	-	-	-	-
BMI	-	-	-	-	-	0.551	-	-
< 18.5	6	-0.30 (-0.76, -0.02)	0.040	53.1	0.059	-	-	-
18.5-25	4	-0.16 (-0.59, 0.28)	0.478	28.6	0.241	-	-	-
Exercise duration	-	-	-	-	-	0.876	-	-
1-12 weeks	6	-0.37 (-0.79 0.06)	0.093	63.2	**0.066**	-	-	-
> 12 weeks	4	-0.20 (-0.51, 0.10)	0.188	0.0	0.484	-	-	-
Exercise intensity	-	-	-	-	-	0.685	-	-
Low	1	-0.45 (-1.48, 0.58)	0.393	-	-	-	-	-
Medium	6	-0.40 (-0.86, 0.05)	0.084	68.3	**0.007**	-	-	-
High	3	-0.22 (-0.58, 0.14)	0.237	0.0	0.066	-	-	-

Notes: p^1 value for net change; p^2 value for heterogeneity in the subgroup; *p*3 value for heterogeneity between groups with meta-regression, analyzed as categorical variables; *p*4 value for publication bias; significant *p*-values are highlighted in bold prints. Abbreviations: BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; IL-6, interleukin 6; TNFα, tumor necrosis factor alpha.

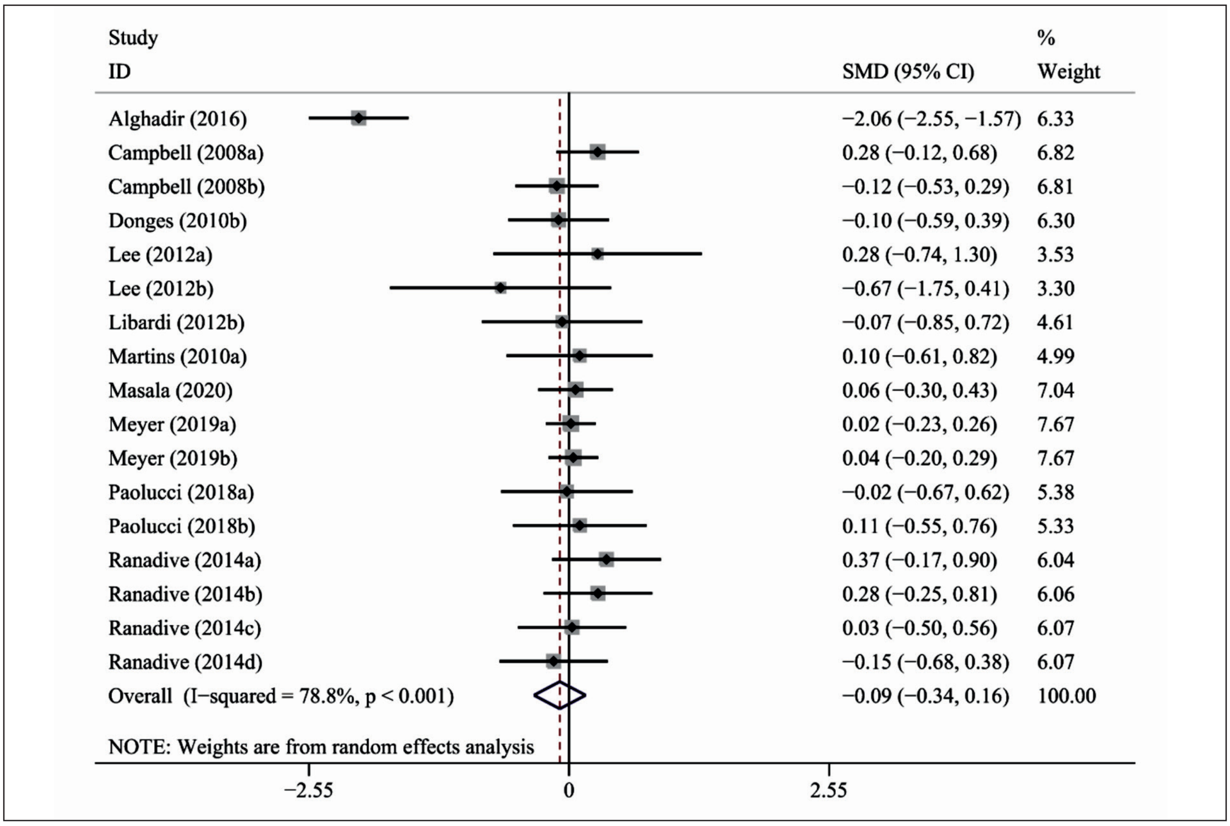

Figure 3. Forest diagram of the effect of aerobic exercise on CRP level of healthy adults.

duce CRP levels. To further explore the source of heterogeneity, univariate meta-regression analysis was used. The results showed that exercise intensity (p = 0.018) and BMI (p = 0.094) could significantly affect the effect of aerobic exercise on CRP levels, suggesting that exercise intensity and BMI may be the source of heterogeneity.

TNFα in Healthy Adults

7 studies[18-20,22,24,25,27] consisting of 10 intervention groups reported the effect of aerobic exercise on TNFα levels in healthy adults. The pooled results showed that aerobic exercise could significantly reduce TNFα levels (SMD = - 0.30, 95% CI: - 0.58 – - 0.03, p = 0.032), and there was no significant heterogeneity (I^2 = 43.9%, p = 0.066) (Figure 4). Sensitivity analysis showed that aerobic exercise could significantly reduce TNFα levels in men (SMD = -0.92, 95% CI: - 1.80 – -0.04, p = 0.040) (Table III).

Publication Bias

Begg's and Egger's tests and funnel plots were used to assess whether there was publication bias for IL-6, CRP and TNFα results. A p-value > 0.05 indicated no statistical difference and no publication bias (Figure 5).

Discussion

Effect of Aerobic Exercise on Inflammatory Factor IL-6 in Healthy Adults

Herein, we showed that aerobic exercise had no significant effects on the level of IL-6, while age, BMI, exercise duration, and exercise intensity could be influencing factors. The subgroup analysis showed that aerobic exercise with a duration > 12 weeks at a moderate intensity could significantly reduce IL-6 levels. Growing evidence suggests that the degree of exercise-induced IL-6 response depends on the intensity of exercise, especially the duration, while the mode of exercise has little effect[28]. This phenomenon may be attributed to the relationship between muscle contraction and IL-6 levels. Moreover, it has been reported that changes in calcium homeo-

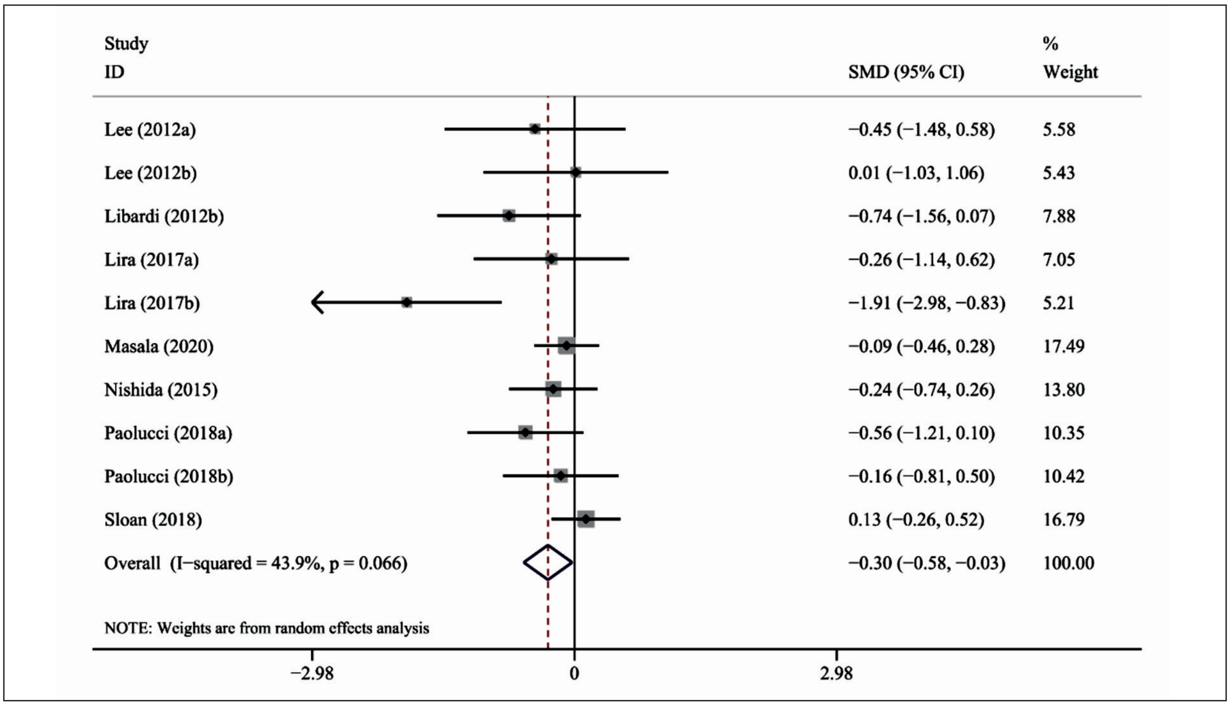

Figure 4. Forest diagram of the effect of aerobic exercise on TNFα level of healthy adults.

stasis, impaired glucose tolerance and increased formation of reactive oxygen species (ROS) can activate transcription factors that regulate IL-6 synthesis.

Effect of Aerobic Exercise on Inflammatory Factor CRP in Healthy Adults

This study substantiated that aerobic exercise had no significant effects on CRP levels. The meta-regression analysis showed that exercise intensity and BMI might be the sources of heterogeneity between studies. Interestingly, it has been reported[23] that aerobic exercise of moderate intensity for 8 and 25 weeks has no significant effect on CRP levels.

Effect of Aerobic Exercise on Inflammatory Factor TNFα in Healthy Adults

Moreover, we found that aerobic exercise could significantly reduce TNFα levels. Sensitivity analysis showed that exercise yielded no effect on TNFα levels. Interestingly, the lowering effect on serum TNFα levels was only observed in the male population. An increasing body of evidence suggests that endurance training and combined

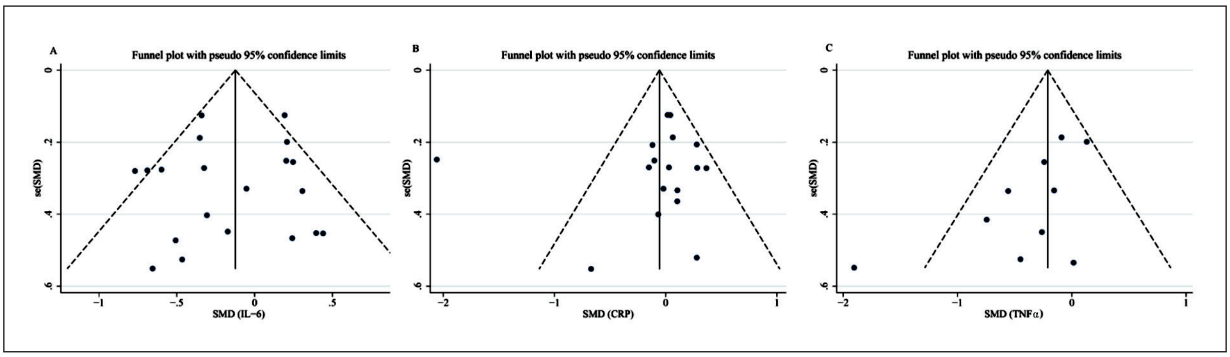

Figure 5. Funnel plot of the effect of aerobic exercise on the level of inflammatory factors in healthy adults.

training of endurance, strength, balance, and flexibility can reduce plasma TNFα levels in healthy elderly people[29]. Moreover, review studies[30] have shown that regular exercise can inhibit TNFα levels, given that IL-6 released by muscle fibers during exercise promotes the production of other anti-inflammatory cytokines and reduces pro-inflammatory cytokine TNFα levels.

Limitations

This study only includes research published in English, which accounted for the limited number of studies included. Among the included literature, only one adopted a blinding method, which may have affected the accuracy of the study findings leading to significant heterogeneity.

Conclusions

Aerobic exercise can significantly reduce TNFα levels in healthy adults, while no significant effect on the levels of IL-6 and CRP was found. Aerobic exercise has a positive preventive effect against inflammatory-related diseases. Future RCTs seeking to explore the value of aerobic exercise should start from moderate intensity exercise for a duration of at least 12 weeks.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Authors' Contribution

Yahai Wang, Donglin Luo, and Haichao Jiang jointly conceived and designed the study. Data collection and analysis were performed by all authors. Yahai Wang, Donglin Luo and Haichao Jiang wrote the first draft of the manuscript. Zhibin Nie, Lin Shao and Haixia Qi edited the manuscript. All authors read and approved the final submitted version.

Ethics Approval and Informed Consent

All analyses were based on previously published studies; thus, no ethical approval and patient consent are required.

Availability of Data and Materials

All the data used in the study can be obtained from the original articles.

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