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RESEARCH

Impact of aerobic exercise on chronic inflammation in older adults: a systematic review and meta-analysis

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Abstract

This study aimed to conduct a systematic review and meta-analysis to investigate the effect of aerobic exercise training on inflammatory markers in older adults. The current literature was searched using PubMed, Scopus, Web of Science, and Google Scholar to identify controlled clinical trials in English. Ten articles met the inclusion criteria. The mean difference (MD) with 95% confidence intervals (CIs) and the overall effect size was calculated for all comparisons. The PEDro scale was used to evaluate the quality of articles. The findings indicated that aerobic exercise training led to an improvement in inflammatory markers in older adults: IL-6 (mean difference = 0.939, $Z = 2.857$, $P = 0.004$), CRP (mean difference = 0.853, $Z = 3.060$, $P = 0.002$), TNF-α (mean difference = 0.705, $Z = 3.094$, $P = 0.002$), IL-10 (mean difference = 1.511, $Z = 2.036$, $P = 0.042$). This review demonstrates that aerobic exercise training significantly improves inflammatory markers in older adults, reducing CRP, TNF-α, and IL-6, while increasing IL-10, with particular benefits for populations at risk for chronic inflammatory diseases. According to the results of this review, an effective aerobic exercise program should include moderate to high intensity (60–80% HRmax or HRR), sessions lasting 30 to 60 min, and a frequency of 2 to 3 times per week.

Keywords Aerobic training, Inflammatory markers, Older adults

Introduction

Current research aims to improve our understanding of the mechanisms of aging and the factors affecting it. The population of individuals aged 65 years and older is projected to increase significantly by 2030, contributing to a growing proportion of older adults globally [1].

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Inflammation is one of the most researched biological mechanisms influencing healthy and pathological aging [2]. Inflammation is a natural physiological process crucial for tissue repair in response to endogenous or exogenous aggressions. Although inflammation is a normal part of the repair response and crucial for protecting us from bacterial and viral infections as well as harmful environmental factors, not all inflammation is beneficial. When inflammation lasts too long and becomes chronic, it can lead to harm and destruction [3]. Chronic inflammation that occurs with aging, often called "inflammaging," poses risks to functional abilities, independence, and overall quality of life for older adults [4]. Inflammaging has been associated with muscle loss, sarcopenia, and related functional impairments in elderly individuals,

probably due to its adverse effects on muscle protein balance [5–8]. Given the strong link between inflammation and the development and progression of numerous age-related chronic conditions, various strategies have been employed to minimize aging-related inflammation. Pharmacological interventions may offer an alternative approach, as medications have been suggested to reduce inflammation potentially. However, the abundance of side effects commonly associated with these drugs, such as gastrointestinal distress and cardiovascular complications, as well as the additional financial burden, have limited the practical utility of these treatments [9]. As a result, lifestyle interventions, such as modifications to exercise training, may offer a long-term and cost-effective solution to mitigate inflammation and delay the progression of aging in the elderly.

Physical exercise is widely recognized as a key strategy for reducing the risk of age-related diseases. Recent research has highlighted the role of aerobic exercise in reducing inflammatory markers in older adults [10]. Aerobic exercise has gained widespread popularity globally due to its accessibility and effectiveness, particularly through time-efficient formats such as exercise snacks, which enhance cardiovascular fitness and overall health in older adults [11]. Furthermore, aerobic exercise, including high-intensity interval training, has been shown to improve body composition and cardiometabolic health in older adults at elevated risk of metabolic syndrome and heart failure, leading to reductions in body fat, improved insulin sensitivity, and enhanced cardiovascular function [12, 13]. Research suggests that exercise can both cause and reduce inflammation. In certain situations, inflammatory cytokines can be found in the peripheral blood of individuals following high-intensity, unaccustomed exercise, particularly when eccentric contractions are involved [14, 15]. This harmful reaction is lessened with repeated exercise as the body adapts to the increased stress [16]. Numerous studies have shown that individuals who engage in frequent and intense exercise tend to have lower concentrations of inflammatory biomarkers [17–20]. A meta-analysis of eight randomized controlled trials (RCTs) also indicated that exercise can reduce the risk of age-related diseases by lowering inflammatory markers in older adults [21]. Additional meta-analyses and systematic reviews have demonstrated that exercise has a beneficial effect on inflammation in patients with chronic diseases, such as breast cancer [22], heart disease [23], and diabetes [20, 24].

However, there is currently no consensus regarding the impact of regular exercise on inflammatory biomarkers in relatively healthy elderly individuals. Some studies have failed to show a significant effect of exercise training on inflammatory biomarkers, including C-reactive protein, interleukin-6, and tumor necrosis factor-alpha receptor 1 in older populations [25–27]. The reasons for this discrepancy may include variations in the type of exercise training (e.g., aerobic vs. resistance training), differences among subjects (e.g., age, sex, health status, and baseline inflammation), and variations in training protocols (such as intensity, frequency, and duration of the intervention).

Given that the available data from studies focused on the effects of aerobic exercise training on inflammation are limited, the findings remain inconclusive. Therefore, this study aimed to evaluate the impact of aerobic exercise training on inflammatory factors in the elderly through a systematic review and meta-analysis of randomized controlled trials.

Methods

This research adhered to the guidelines established by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). The protocol for this systematic review was registered prospectively in the PROSPERO database with the registration number CRD42024574233.

Search strategy

An extensive literature review was conducted across multiple electronic databases, such as PubMed, Web of Science, and Scopus, to identify studies suitable for inclusion. This review covered the period from establishing these databases up to April 4, 2024, utilizing a variety of combinations of Medical Subject Headings (MeSH) and free-text keywords pertinent to exercise training, inflammatory biomarkers, and age. The search was deliberately unrestricted in terms of geographical scope or publication type. Furthermore, the reference lists of the obtained studies were scrutinized to identify additional relevant articles. The search strategies employed were as follows: ("exercise" or "exercise training" or "aerobic exercise" or "aerobic training" or "resistance training" or "resistance exercise" or "physical activity") AND ("inflammatory markers" or "inflammatory factors" or "C-Reactive protein" or "CRP" or "Fibrinogen" or "Procalcitonin" or "ESR" or "Interleukin" or "Tumor necrosis factor" or "Ferritin" or "Cortisol" or "Plasma viscosity") AND ("older adults" or "elderly" or "aging"). This methodology aimed to enhance the outcomes and intersect the primary terms to maximize the number of studies retrieved.

Inclusion criteria

The review encompassed studies that adhered to specific criteria: (1) Study Design: Only randomized controlled trials (RCTs) were included; (2) Participants: The emphasis was on older adults aged 65 years and older who may have various diseases or medical conditions; (3) Intervention: The experimental group was required to participate in any form of aerobic exercise training or a combination

of aerobic exercise training with non-exercise interventions for at least two weeks; (4) Control: The control group was not involved in any exercise interventions beyond their regular activities and sham exercises (such as stretching or balance training); (5) Outcomes: The studies were required to assess at least one inflammatory marker in serum or plasma. Studies that were not published in English or did not provide accessible data were excluded from the review.

Exclusion criteria

Studies were excluded from consideration if they fulfilled any of the following criteria: (1) they involved multiple interventions, such as a combination of diet and exercise or the use of nutritional supplements in conjunction with exercise; (2) they compared different types of exercise, such as aerobic training versus resistance training, without the inclusion of a control group; (3) they evaluated physical activity against aerobic exercise training modalities, such as jogging compared to aerobic training, again without a control group; (4) they lacked adequate data necessary for conducting meta-analyses, such as mean values and standard deviations.

Study selection and data extraction

In the preliminary screening stage, all collected records were imported into reference management software (Endnote21) to eliminate duplicates and evaluate potential eligibility by reviewing titles and abstracts. Subsequently, a thorough examination of the complete texts was performed. Any discrepancies were resolved by a designated reviewer (DH). Data extraction was conducted by one reviewer utilizing a standardized form, which was later validated by another reviewer (HP). The data extracted included information such as the primary author's name, characteristics of the study (including the year of publication, study design, and methodological details), characteristics of the participants (such as average age and sample size), and specific details regarding the interventions for both the experimental and control groups (including duration, frequency, intensity, and type of combined exercise), as well as the outcome results.

Assessment of risk of bias of included studies

The assessment of bias risk in the studies incorporated in the review was performed by two independent reviewers (DH and HP) using the Cochrane Collaboration tool, as described by Higgins et al. [28] in 2024. This tool consists of seven essential items organized into six separate domains: (1) selection bias, which encompasses random sequence generation and allocation concealment; (2) performance bias, which emphasizes the blinding of both participants and personnel; (3) detection bias, concerning the blinding of those assessing outcomes; (4) attrition bias, associated with incomplete outcome data; (5) reporting bias, which deals with selective reporting; and (6) other biases. Each study was assessed against each specific item, and the domains were classified as "low," "high," or "unclear," depending on whether they met the evaluation criteria defined by the respective items. When disagreements emerged during the evaluation, a third reviewer (SMT) was consulted to provide clarification.

Data analysis

Statistical evaluations were performed utilizing the Comprehensive Meta Analysis V3 software suite. A meta-analytical approach was employed to examine the changes in inflammatory markers from baseline measurements to those recorded post-intervention. This was achieved by calculating the mean difference (MD) between the experimental and control cohorts, accompanied by a 95% confidence interval (CI). The MD and standard error (SE) for each inflammatory marker were computed before and after the intervention using Morris's formula [29, 30]. In scenarios where data were reported as means accompanied by 95% CIs, the standard deviation (SD) was extracted through the functionalities of the RevMan software. Conversely, in cases where data were articulated as median interquartile ranges (IQR), the mean and SD were derived following the methodologies proposed by Wan et al. [31] and Luo et al. [32]. For studies reporting only changes in inflammatory markers, we contacted the authors to obtain the original datasets. Data were amalgamated for the meta-analysis when two or more studies reported identical outcomes and provided data in compatible formats. The heterogeneity among the included studies was assessed using the χ^2 test alongside the Higgins I^2 statistic, with a significance threshold set at $P < 0.05$. The pooled effect was determined using a fixed-effect model when the data were available, and no significant heterogeneity was detected; otherwise, a random-effects model was employed.

Results

Figure 1 provides a visual overview of the search results. This study began by gathering a large pool of potential research articles from three major databases: PubMed (1384), Web of Science (1733), and Scopus (2247). After removing duplicate entries, over 3900 articles remained. The researchers then carefully reviewed these articles, focusing on their titles, abstracts, keywords, and full text. This process narrowed the selection to 17 articles that met inclusion criteria and had enough data for analysis. These 17 studies, with details like the number of participants, gender, interventions used, and key findings, are summarized in Table 1. Also, by evaluating the quality of the selected articles, it was found that the average PEDro scale of articles is 6.29.
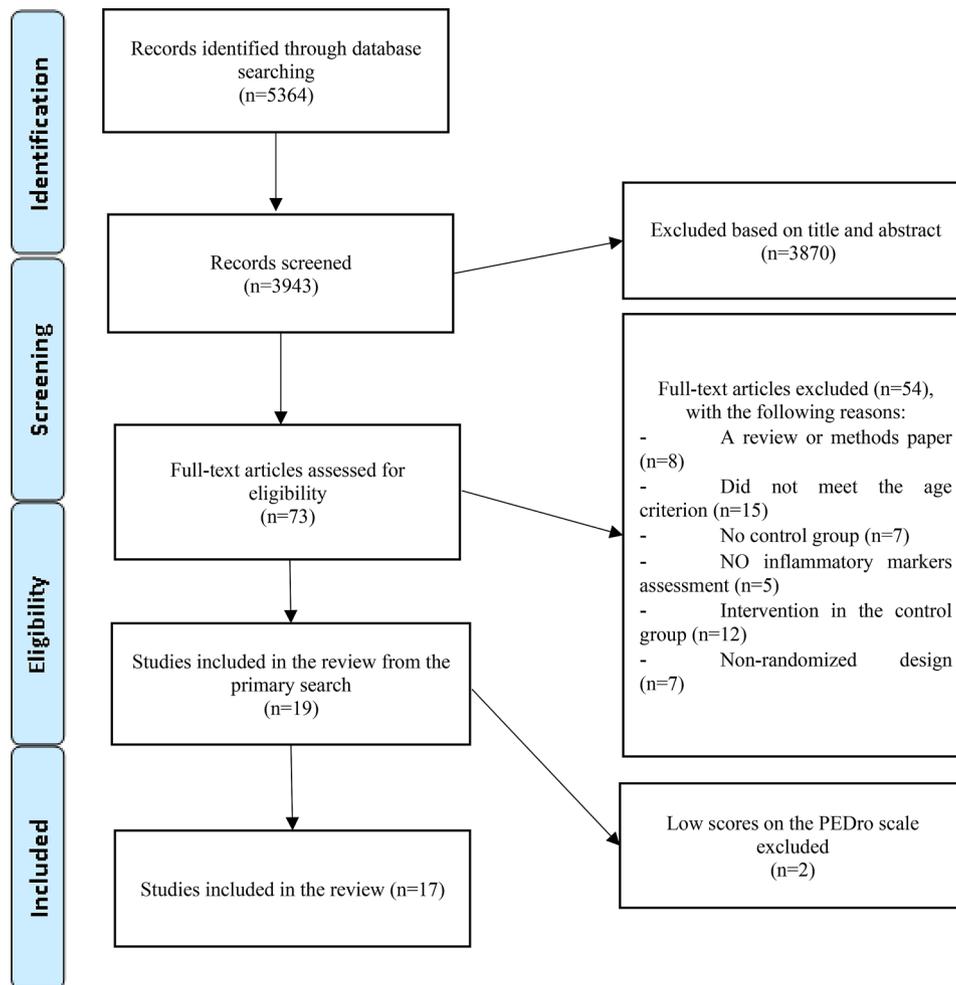
Fig. 1 Flow diagram regarding article selection for the meta-analysis

Effects of aerobic exercise training on IL-6

A total of 9 studies were analyzed to assess the impact of aerobic exercise training on IL-6 levels. The findings indicated that aerobic exercise training reduced IL-6 (mean difference = 0.939, $Z = 2.857$, $P = 0.004$; Fig. 2) compared to the control group. The studies exhibited moderate and significant heterogeneity ($I^2 = 87.69\%$, $p = 0.000$). Visual analysis of funnel plots does not indicate potential publication bias, supported by Begg's test ($P = 0.175$) and Egger's ($p = 0.050$). The trim and fill method revealed four studies likely missing from the left side of the plot. The sensitivity analysis was assessed using one study-removed method. Removing any individual study indicated a low risk of bias, and the results of the meta-analysis remained stable without significant changes.

Effects of aerobic exercise training on CRP

A total of 10 studies were analyzed to assess the impact of aerobic exercise training on CRP levels. The findings indicated that aerobic exercise training reduced CRP (mean difference = 0.853, $Z = 3.060$, $P = 0.002$; Fig. 3) compared

to the control group. The studies exhibited moderate and significant heterogeneity ($I^2 = 86.97\%$, $p = 0.000$). Visual analysis of funnel plots does not indicate potential publication bias, supported by Begg's test ($P = 0.858$) and Egger's ($p = 0.063$). The trim and fill method revealed six studies likely missing from the left side of the plot. The sensitivity analysis was assessed using one study-removed method. Removing any individual study indicated a low risk of bias, and the results of the meta-analysis remained stable without significant changes.

Effects of aerobic exercise training on TNF-α

A total of 8 studies were analyzed to assess the impact of aerobic exercise training on TNF-α levels. The findings indicated that aerobic exercise training reduced TNF-α (mean difference = 0.705, $Z = 3.094$, $P = 0.002$; Fig. 4) compared to the control group. The studies exhibited moderate and significant heterogeneity ($I^2 = 76.54\%$, $p = 0.000$). Visual analysis of funnel plots does not indicate potential publication bias, supported by Begg's test ($P = 0.500$) and Egger's ($p = 0.124$). The trim and fill method revealed

Table 1 Specifications of the analyzed randomized controlled trials

Study	Total sample size/gender	Population (Country)	Intervention		Results	PEDro score
			Duration (week)	Session per week		
Abd El-Kader and Al-Jiffri 2019 [33]	50/ Male: - Female: -	Previously sedentary elderly subjects / Saudi Arabia	24/6 months	3	The mean values of TNF- α, and IL-6 decreased significantly, and the mean value of IL-10 significantly increased in the group (A) after the aerobic exercise training	7
Alghadir and Gabr 2020 [34]	80 / Male: 50 Female: 30	Older Adults with Depression / Saudi Arabia	12	3	In older adults exhibiting elevated depressive scores, there was a notable alteration in the concentration of adrenal hormones when compared to the control group. Specifically, there was a substantial rise in the levels of adrenocorticotropic hormone (ACTH), cortisol, and the cortisol to dehydroepiandrosterone sulfate (DHEA/S) ratio, alongside a reduction in DHEA/S levels.	7
Alghadir et al. 2016 [35]	100/ Male:65 Female: 35	Healthy older adults / Saudi Arabia	24	3	Individuals who engage in regular physical activity demonstrated enhanced cognitive performance, accompanied by lower concentrations of malondialdehyde (MDA), 8-hydroxy-2'-deoxyguanosine (8-OHdG), and high-sensitivity C-reactive protein (hs-CRP), as well as elevated total antioxidant capacity (TAC) activity when compared to those who lead a sedentary lifestyle.	8
Byrkjeland et al. 2011 [36]	80/ Male: 63 Female: 17	Patients with chronic heart failure / Norway	16 / 4 months	2	No significant differences in changes between the EX group and the CON group were obtained in any of the measured variables, such as CRP, TNF-α, IL-6, VCAM-1, ICAM-1, and TGF-β, except in patients with idiopathic dilated cardiomyopathy (IDCM), where significant reductions in CRP, ICAM-1, TGF-β and TNF-α levels were observed ($p < 0.05$ for all).	7
Dong-Hyun et al. 2019 [37]	36/ Male: - Female: 36	Pre-frailty older women with hypertension/ South Korea	12	3	Tumor necrosis factor-a ($p = 0.000$), high-sensitivity C-reactive protein ($p = 0.000$) showed a valid difference in the interaction between the group and time.	6
Jensen et al. 2019 [38]	198/ Male:113 Female:85	Patients with Alzheimer's disease/Denmark	16	3	Most inflammatory markers remained unchanged after exercise. There was an increasing effect of 16 weeks of physical exercise on sTREM2 measured in CSF.	7
Lima et al. 2015 [39]	29/ Male: 3 Female: 26	Hypertensive older adults/ Brazil	10	3	Aerobic exercise produced the reduction of plasma IL-6 levels	4
Martins et al. 2010 [40]	45/ Male: 18 Female: 27	Elderly population/ Portugal	16	3	hs-CRP concentrations were maintained throughout the study for the C group while decreasing 10% at 16 weeks and 51% at 32 weeks for the AT group	6
McDermott et al. 2004 [41]	32/ Male: - Female: -	Men and women with peripheral arterial disease / USA	12	-	There were no significant changes in the inflammatory blood factors after exercise	5
Morawin et al. 2021 [42]	80/ Male: 8 Female: 72	older adults/ Poland	40 / 10 months	2	Tai-Chi training elevated the plasma levels of C-reactive protein (CRP), tumor necrosis factor (TNFα), and tumor necrosis receptor factor II (TNFRII) and decreased caspases 8 and 9	6
Muscari et al. 2010 [43]	120/ Male: 62 Female: 58	Healthy older adults/	48 / 12 months	3	CRP decreased only in the treatment group.	8
Osali 2020 [44]	44 females	Elderly females with metabolic syndrome/ Iran	6	1	IL-10 and BDNF concentrations significantly increased after a 6-week intervention ($P \leq 0.05$). Also, IL-6 serum levels significantly decreased ($P \leq 0.05$).	5
Petersen et al. 2008 [45]	39/ Male: 16 Female: 22	Chronic obstructive pulmonary disease patients and healthy patients / Denmark	7	2	Training did not affect the plasma concentration of inflammatory markers but decreased leucine R(a) in subjects with COPD by approximately 10% ($P < 0.05$	5

Table 1 (continued)

| Study	Total sample size/gender	Population (Country)	Intervention		Results	PEDro score
			Duration (week)	Session per week		
Rejeski et al. 2019 [46]	222/ Male: 64 Female: 158	Older Adults who are Overweight or Obese and have Cardiometabolic Disease/ USA	72 / 18 months	During the initial intensive phase,3 group sessions and one individual session each month/1 monthly session during the transition and maintenance phase,	CRP values in WL + RT were significantly lower than in WL.The only difference in IL-6 was that, at 18-months, WL + RT was lower than WL + AT	7
Ruangthai and Phoemsapthawee 2019 [47]	54/ Male: 11 Female: 43	Elderly individuals with hypertension/ Thailand	12	3	hs-CRP concentrations decreased by 49.2% in only the CBT	6
Sungkarat et al. 2018 [48]	66/ Male: 9 Female: 57	Older Adults With Mild Cognitive Impairment/ Thailand	24 / 6 months	3	TNF-α and IL-10 measures were similar between the two groups	6
Wanderley et al. 2013 [49]	50/ Male: 11 Female: 39	Older adults/ Portugal	32 / 8 months	3	Along with a change in hs-CRP (-18.6 ± 60.6%), in response to aerobic training	7
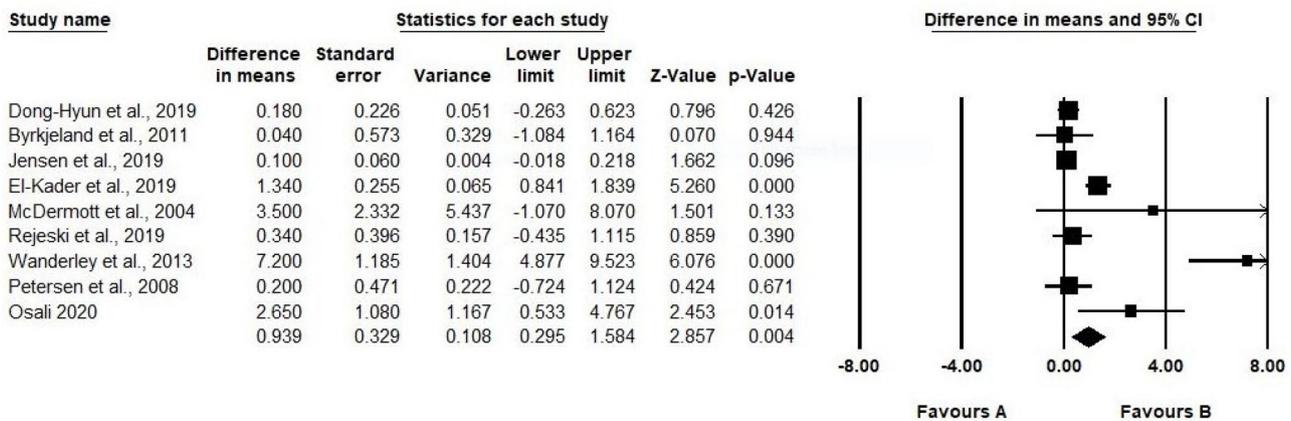
Fig. 2 Meta-analysis of the effects of aerobic exercise training on IL-6 in older adults

three studies likely missing from the left side of the plot. The sensitivity analysis was assessed using one study-removed method. Removing any individual study indicated a low risk of bias, and the results of the meta-analysis remained stable without significant changes.

Effects of aerobic exercise training on IL-10

A total of 4 studies were analyzed to assess the impact of aerobic exercise training on IL-10 levels. The findings indicated that aerobic exercise training increased IL-10 (mean difference = 1.511, Z = 2.036, $P = 0.042$; Fig. 5)

compared to the control group. The studies exhibited moderate and significant heterogeneity ($I^2 = 91.31\%$, $p = 0.000$). Visual analysis of funnel plots does not indicate potential publication bias, supported by Begg's test ($P = 0.734$) and Egger's ($p = 0.218$). The trim and fill method revealed two studies that were likely missing from the left side of the plot. The sensitivity analysis was assessed using one study-removed method. Removing any individual study indicated a low risk of bias, and the results of the meta-analysis remained stable without significant changes.
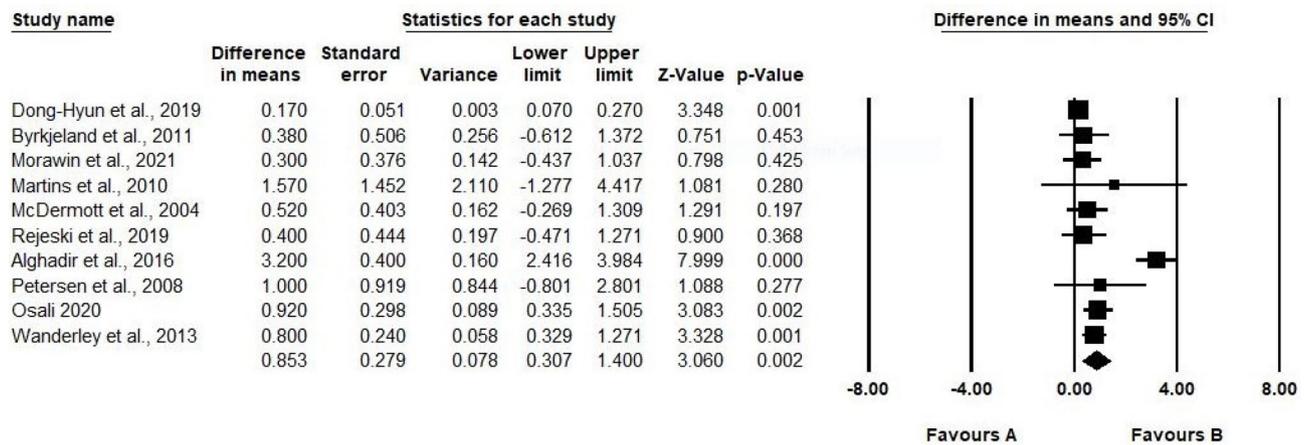
Study name	Statistics for each study							Difference in means and 95% CI
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Dong-Hyun et al., 2019	0.170	0.051	0.003	0.070	0.270	3.348	0.001	
Byrkjeland et al., 2011	0.380	0.506	0.256	-0.612	1.372	0.751	0.453	
Morawin et al., 2021	0.300	0.376	0.142	-0.437	1.037	0.798	0.425	
Martins et al., 2010	1.570	1.452	2.110	-1.277	4.417	1.081	0.280	
McDermott et al., 2004	0.520	0.403	0.162	-0.269	1.309	1.291	0.197	
Rejeski et al., 2019	0.400	0.444	0.197	-0.471	1.271	0.900	0.368	
Alghadir et al., 2016	3.200	0.400	0.160	2.416	3.984	7.999	0.000	
Petersen et al., 2008	1.000	0.919	0.844	-0.801	2.801	1.088	0.277	
Osali 2020	0.920	0.298	0.089	0.335	1.505	3.083	0.002	
Wanderley et al., 2013	0.800	0.240	0.058	0.329	1.271	3.328	0.001	
	0.853	0.279	0.078	0.307	1.400	3.060	0.002	

Fig. 3 Meta-analysis of the effects of aerobic exercise training on CRP in older adults

Study name	Statistics for each study							Difference in means and 95% CI
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Dong-Hyun et al., 2019	0.740	0.188	0.035	0.372	1.108	3.945	0.000	
Byrkjeland et al., 2011	0.090	0.412	0.170	-0.717	0.897	0.219	0.827	
Morawin et al., 2021	0.700	0.366	0.134	-0.017	1.417	1.912	0.056	
Jensen et al., 2019	0.200	0.072	0.005	0.060	0.340	2.791	0.005	
El-Kader et al., 2019	2.130	0.417	0.174	1.312	2.948	5.106	0.000	
Sungkarat et al., 2018	0.300	1.003	1.006	-1.666	2.266	0.299	0.765	
Petersen et al., 2008	0.800	0.364	0.133	0.087	1.513	2.198	0.028	
Wanderley et al., 2013	0.900	1.525	2.326	-2.089	3.889	0.590	0.555	
	0.705	0.228	0.052	0.258	1.151	3.094	0.002	

Fig. 4 Meta-analysis of the effects of aerobic exercise training on TNF-α in older adults

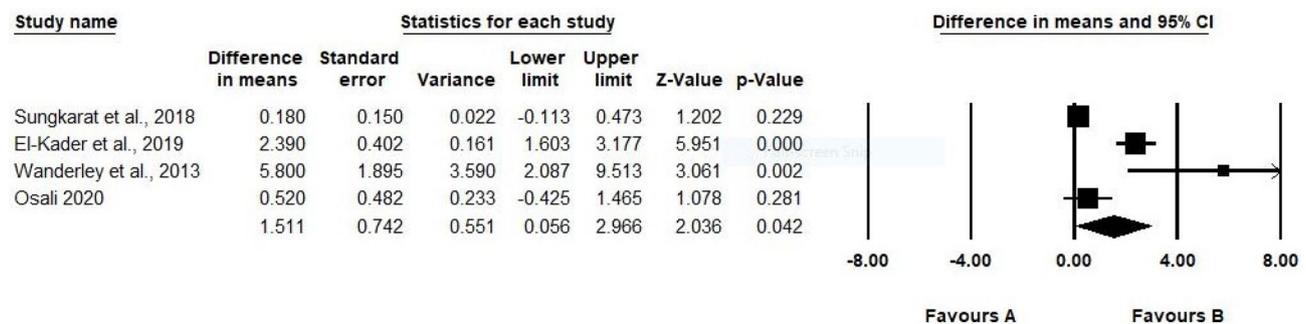| Study name	Statistics for each study							Difference in means and 95% CI
	Difference in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Sungkarat et al., 2018	0.180	0.150	0.022	-0.113	0.473	1.202	0.229	
El-Kader et al., 2019	2.390	0.402	0.161	1.603	3.177	5.951	0.000	
Wanderley et al., 2013	5.800	1.895	3.590	2.087	9.513	3.061	0.002	
Osali 2020	0.520	0.482	0.233	-0.425	1.465	1.078	0.281	
	1.511	0.742	0.551	0.056	2.966	2.036	0.042	

Fig. 5 Meta-analysis of the effects of aerobic exercise training on IL-10 in older adults

Discussion

This meta-analysis aimed to systematically evaluate the effects of regular aerobic exercise training on inflammatory biomarkers in older adults. In this review, we included seventeen randomized controlled trials involving 1,325 participants, which compared the effects of aerobic exercise training interventions against control groups. To provide context, our findings resonate with recent explorations into exercise effects across diverse populations, particularly where nontraditional high-intensity interval training (HIIT) has been emphasized. Studies have shown that such training approaches can lead to significant enhancements in anthropometric characteristics, such as reduced waist circumference, and improvements in body composition, including lower fat mass and better muscle preservation [50]. Furthermore, evidence highlights benefits in psychological health, with noted improvements in mood stability and cognitive function, alongside gains in physical performance, such as increased strength and endurance [51]. For

cardiometabolic health, reductions in key risk factors like blood pressure and insulin resistance have been observed, supporting positive outcomes in adults worldwide, from healthy individuals to those with chronic conditions [52]. These insights align with our results, suggesting that tailored exercise strategies, including nontraditional HIIT, could broadly enhance inflammation management in older adults. The results indicate that regular aerobic exercise training significantly improves many inflammatory factors in older adults, including CRP, TNF-α, IL-6, and IL-10. However, further studies are necessary to validate the findings related to IL-10.

There are significant associations between inflammation and the aging process. Prospective epidemiological studies indicate heightened baseline inflammation is linked to an increased risk of chronic diseases commonly associated with aging [53–56]. Aging is associated with chronic low-grade inflammation, characterized by elevated levels of inflammatory markers such as interleukin-6 (IL-6) and C-reactive protein (CRP) in the bloodstream [57].

Exercise is widely recognized as an effective non-pharmacological method for modulating systemic inflammation in individuals with existing diseases and healthy populations. However, many previous reviews have focused primarily on the effects of exercise on inflammation in diseased individuals [58–61]. A systematic review suggested that aerobic and resistance exercises might reduce levels of cytokines, including IL-6, CRP, and TNF-α, in older adults [62]. However, an earlier meta-analysis found that while regular exercise could lower CRP and IL-6 levels, it had no significant effect on TNF-α in the older population [21]. A recent study examined the effect of aerobic exercise training on inflammatory factors and reported that aerobic exercise training can significantly reduce TNFα levels in healthy adults [63].

In contrast, no significant impact on the levels of IL-6 and CRP was observed [63]. Some studies included in the present meta-analysis have indicated that inflammatory markers α-TNF, -6IL, and CRP significantly decreased after aerobic exercise training [36, 37, 45, 49]. On the other hand, several studies have examined the impact of aerobic exercise training on the levels of the anti-inflammatory factor IL-10. Some of these studies indicate a significant increase in IL-10 levels following 6 weeks [44] and 6 months of aerobic exercise training in elderly individuals [33]. However, Sungkarat et al. reported a considerable decrease in IL-10 levels after 6 months of tai chi training [48], while Wanderly et al. noted a significant reduction in IL-10 levels after 8 weeks of aerobic training [49]. Variability in results can be attributed to differences in study design, sample sizes, exercise protocols (including intensity and duration), and methodological diversity among the studies included. These inconsistencies

underscore the necessity for further investigation, prompting the current study to thoroughly evaluate a more uniform set of parameters and populations.

The exact mechanisms by which physical activity reduces inflammation are not fully understood. One possible mechanism for the effects of exercise training on improving inflammation is the intracellular signaling pathways mediated by nitric oxide. Nitric oxide is closely related to the inflammatory state and is an important mediator of inflammation. The enzyme nitric oxide synthase (eNOS) regulates the expression of proinflammatory molecules such as nuclear factor-κB and cyclooxygenase-2, as well as proinflammatory cytokines. Nitric oxide derived from eNOS plays an important role in some of the fundamental events of inflammation, such as cell adhesion, modulation of vascular permeability, and angiogenesis. Notably, after moderate-intensity exercise, nitric oxide levels increase, leading to improved muscle performance and reduced inflammation [64]; exercise also reduces the production of proinflammatory cytokines (α-TNF and α-IL-1) by mononuclear cells while increasing the production of anti-inflammatory cytokines (IL-10, IL-4, and TGF-β-1) [65]. Exercise reduces the amount of α-TNF produced by monocytes, CD14 + and CD16 + monocytes [66]; exercise also reduces the expression of the monocyte cell-level Toll-like receptor 4, which is a lipopolysaccharide signaling receptor and helps attenuate acute immune responses to infection or trauma [67, 68]; therefore, the results of these studies suggest that in response to repeated muscle contractions, There is negative regulation of cytokine production from immune cells [69]. In addition, possible mechanisms of the anti-inflammatory effects of exercise training include a decrease in body fat percentage, accumulation of macrophages in adipose tissue, inhibition of α-TNF, IL-6 released from muscles, and cholinergic anti-inflammatory pathways. Factors released following exercise training, such as glucocorticoids or other stress hormones (e.g., epinephrine) or IL-6, decrease acute inflammation in response to inflammatory conditions, including chronic obstructive pulmonary disease. Another possible mechanism is the effect of exercise training on reducing inflammation, leptin, and adipocytes, and ultimately, reducing inflammatory cytokines and inhibiting inflammatory pathways [70–72].

Future studies should aim to resolve the discrepancies regarding the impact of aerobic exercise training on different inflammatory biomarkers. Researchers should investigate the biological mechanisms involved and determine optimal exercise parameters to enhance health benefits for older adults. Furthermore, exploring the connections between inflammation, exercise, and age-related diseases may induce new insights into utilizing exercise

as a preventive and therapeutic strategy in the care of the elderly.

Conclusions

This review demonstrates that aerobic exercise training significantly benefits CRP, TNF-α, IL-6, and IL-10 levels. The evidence suggests that the anti-inflammatory effects of aerobic exercise training may go beyond immediate reductions in these markers, contributing to long-term changes in the immune response. This is especially important for populations at risk for chronic inflammatory diseases, such as older adults and individuals with metabolic disorders. Additionally, the results of this meta-analysis suggest that an effective aerobic exercise training program should include moderate to high intensity (60 to 80% of HRmax or HRR), sessions lasting 30 to 60 min, and a frequency of 2 to 3 sessions per week. As such, incorporating aerobic exercise training into public health recommendations is essential as an effective strategy for improving overall health and reducing inflammation.

Author contributions
DH and HP were major contributors to writing the manuscript. SMT was the supervisor and edited the manuscript. MA and AS contributed to the drafting of the article and the methodology. All the authors gave final approval of the version to be submitted.

Data availability
The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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