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Effects of Resistance Training on Interleukin-6 and Tumor Necrosis Factor-Alpha in Older Adults: A Systematic Review

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ABSTRACT

Inflammaging is a chronic low-grade inflammatory condition that contributes to sarcopenia and functional decline in older adults, primarily through elevated interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α). Resistance training has been proposed as a non-pharmacological strategy with potential anti-inflammatory effects. However, evidence from randomized controlled trials (RCTs) remains inconsistent. This systematic review aimed to examine the effects of resistance training on IL-6 and TNF-α levels in adults aged ≥60 years. The review was conducted in accordance with PRISMA guidelines employing a narrative synthesis approach. RCTs published between 2010 and 2024 were retrieved from PubMed, Cochrane, and Scopus. Eight RCTs met the inclusion criteria. Four studies (50%) reported significant reductions in IL-6, while five studies (62.5%) demonstrated significant reductions in TNF-α. Pure resistance training showed greater consistency in reducing TNF-α compared to IL-6. Effective training protocols typically lasted 8–24 weeks, with a frequency of 2–3 sessions per week and intensities ranging from 60–80% of one-repetition maximum (1RM). Resistance training appears to be effective in attenuating inflammatory biomarkers in older adults, particularly TNF-α. However, outcomes are influenced by exercise modality, duration, intensity, and participant characteristics. Further studies using standardized protocols and longer follow-up periods are warranted.

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INTRODUCTION

Population aging is one of the most significant demographic transformations in the 21st century. The number of global older adults is expected to reach 1.4 billion by 2030 and continue to increase until 2050 (World Health Organization, 2017). The aging process is characterized by various physiological and biochemical changes, one of which is the appearance of chronic low-level inflammation known as inflammaging (Shive and Pandiyan, 2022). This condition plays an important role in the development of age-related diseases, including sarcopenia (Tylutka, Walas, and Zembron-Lacny, 2024).

Inflammaging is characterized by an increase in proinflammatory cytokines, specifically interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which contribute to a decrease in skeletal muscle mass and function (Li, Liu, and Xie., 2017; Tylutka et al., 2024). High levels of IL-6 correlate with an increased risk of mortality and decreased quality of life, while TNF-α acts as a major regulator of inflammation that accelerates the process of muscle degradation (Tylutka et al., 2024). Sarcopenia, as the main consequence of inflammation, has implications for decreased physical function, increased risk of falls, disability, and mortality in older adults (Batsis and Villareal, 2018; Larsson et al., 2019). Higher levels of IL-6, CRP, and TNF-α are associated with decreased muscle mass and strength. In chronic inflammatory conditions, CRP and IL-6 are reported to correlate positively with total fat mass and negatively correlate with skeletal muscle mass (Alemán et al., 2011; Mikkelsen et al., 2013).

Resistance training has been recognized as one of the effective non-pharmacological interventions to increase muscle mass and strength in older adults (Grgic et al., 2020). In addition to neuromuscular benefits, resistance training has also been reported to have anti-inflammatory effects through cytokine regulation, including the role of IL-6 as a myokine that is antagonistic to TNF-α during physical activity (Santiago et al., 2018). However, evidence from randomized controlled trials on the effects of resistance training on IL-6 and TNF-α levels in older adults is still inconsistent. Some studies show significant reductions in IL-6 and TNF-α levels after resistance training (Heo and Jee, 2024; Tomeleri et al., 2016), while other studies reported that the results were different and did not find a significant effect (Azizbeigi et al., 2015; Calle and Fernandez, 2010; Franceschi and Campisi, 2014; Sellami et al., 2021). To date, there has been no recent systematic review (2010–2024) that specifically evaluates resistance training as the primary intervention against both inflammatory biomarkers simultaneously. In addition, comprehensive mapping of resistance training protocol variations and their relationship to changes in IL-6 and TNF-α is still limited. Based on this background, this study aimed to systematically review the effects of resistance exercise on IL-6 and TNF-α levels in older adults aged ≥60 years, as well as identify the characteristics of the most effective exercise protocols in the context of prevention and management of inflammation.

METHODS

This study is a systematic review prepared according to the guidelines of Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). The data analysis was carried out using a narrative synthesis approach considering the heterogeneity of the intervention design, participant characteristics, and biomarker measurement methods.

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Literature Research Strategy

Literature searches were conducted on three electronic databases, namely PubMed, Cochrane, and Scopus, with a publication range of 2010–2024. The search strategy used a combination of MeSH terms and keywords related to resistance training, older adults, IL-6, TNF-α, and inflammaging. The filters included human studies, RCTs, and English-language publications. Grey literature was not included. The review protocol was not registered in PROSPERO, which is acknowledged as a limitation.

The following is an example of a complete search string used in the PubMed database: (("Resistance Training"[MeSH] OR "Strength Training" OR "Resistance Exercise" OR "Weight Lifting" OR "Weight-Bearing Exercise") AND ("Aged"[MeSH] OR "Older Adults" OR older adults OR "Aging Population") AND ("Interleukin-6"[MeSH] OR "IL-6" OR "B-Cell Stimulatory Factor 2" OR BSF-2) AND ("Tumor Necrosis Factor-alpha"[MeSH] OR "TNF-alpha" OR TNFα) AND ("inflammaging" OR "low-grade inflammation")).

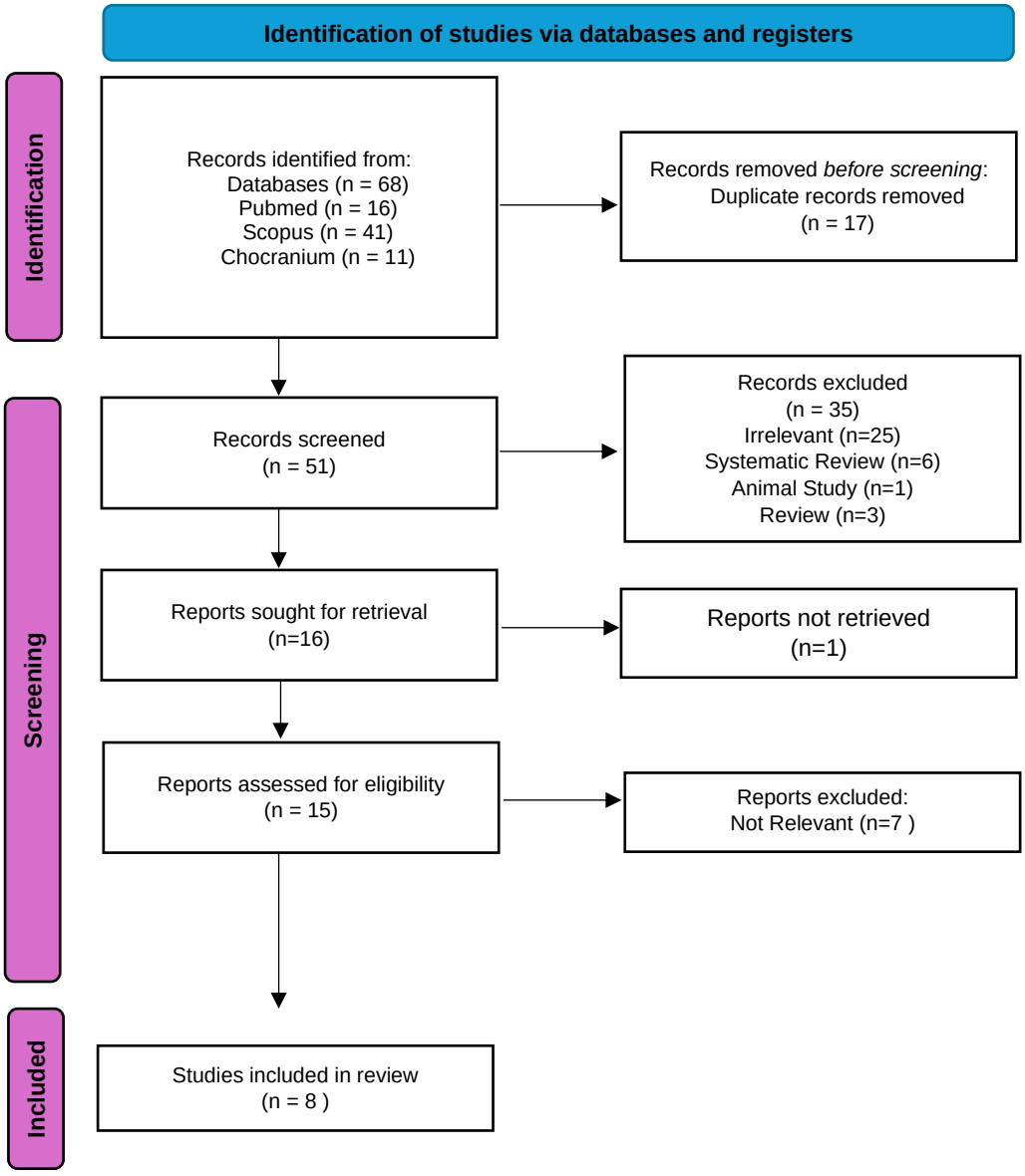

Figure 1. Prisma Flowchart

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Study Selection

All of the obtained articles were imported into Rayyan's software. The selection process was carried out in a double-blind manner by three independent reviewers through three stages, namely elimination of duplication, screening of titles and abstracts, and assessment of full texts. Disagreements were resolved through discussions or by involving the fourth reviewer (SS). The study selection process is described in detail in Figure 1. This systematic review focused on Randomized Controlled Trials (RCTs).

Criteria

The included studies were RCTs in humans with older adult subjects aged ≥60 years, using resistance training as the primary intervention for a minimum of four weeks, having a comparison group, and reporting changes in IL-6 and/or TNF-α levels quantitatively. Non-RCT studies, acute studies, animal studies, as well as studies with combined interventions with no separation of effects were excluded.

Study Quality Assessment

The methodological quality of the study was assessed using the PEDro (Physiotherapy Evidence Database) scale. Scores were classified into high quality (≥6), medium quality (4–5), and low quality (≤3). Assessments were conducted independently by three reviewers who assessed the risk of bias in each included study using the PEDro scale. In case of disagreement, the fourth author (SS) was consulted.

Protocol

Table 1. PICO Framework

Components	Description
P (Population)	Older adults (≥60 years), healthy or with a stable mild inflammatory condition (without organ complications)
I (Intervention)	Resistance training in various forms with a duration of ≥4 weeks
C (Comparison)	No exercises, regular activities, or other types of exercise
O (Outcome)	Changes in levels of IL-6 and/or TNF-α
Study Design	Randomized Controlled Trials (RCTs)

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria are formulated based on the PICO framework.

Table 2. Inclusion and Exclusion Criteria

No.	Criteria	Inclusions	Exclusions
1.	Study type	Randomized Controlled Trials (RCTs) - Human studies	Animal (in vivo) or cell (in vitro) studies- non-RCTs (observational, review, etc)- Acute studies (1 RT session only)
2.	Subject	Age ≥60 years (older adults), healthy or with related inflammatory/ageing	Age <60 years-populations with severe disease (such as cancer, kidney failure, autoimmune, post-transplant)

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No.	Criteria	Inclusions	Exclusions
		conditions (such as sarcopenia, pre-frailty, diabetes, hypertension)	
3.	Intervention	Resistance training as the main intervention-Duration ≥4 weeks-Various forms of RT	The main intervention was not RT (such as dominant aerobics); RT was combined with other interventions without separation of effects (such as diet + RT without separate analysis)
4.	Comparator	No exercise (sedentary), usual care, other exercises (aerobics, stretching) as a comparison group	There is no comparison group at all or not clear
5.	Outcome	At least measure IL-6 and/or TNF-α quantitatively	Not quantitatively reporting IL-6 or TNF-α, only reporting other biomarkers (such as only CRP)
6.	Language	English, publications 2010-2024	In addition to English, before 2010

RESULTS

Characteristics of Included Studies

A total of eight RCT studies with a total of 338 participants were included. The average age of the participants was 69 years, with a predominance of women (89.5%). Exercise protocols vary in duration (8 weeks–8 months), frequency (2–3 sessions/week), and intensity (50–80% 1RM).

Methodological Quality of Studies

Methodological quality was assessed using the PEDro scale, with scores ranging from 4 to 7. Three studies were of good quality (score 7–8) (Tomeleri et al., 2016; Tomeleri et al., 2018; Vasconcelos et al., 2020). Five studies were of fair quality (score 4-5) (Chen et al., 2018; Hangelbroek et al., 2018; Lima et al., 2015; Phillips et al., 2012; Wanderley et al., 2013). None of the studies was of poor quality. The scores of all studies are described in Table 4. The majority of studies had small sample sizes and a follow-up duration of less than 6 months, which limited the generalization of findings.

Effects of Resistance Training on IL-6 and TNF-α

a. IL-6

Of the eight studies analyzed, five studies (50%) reported a significant decrease in interleukin-6 (IL-6) levels after the exercise intervention (Lima et al., 2015; Tomeleri et al., 2016, Tomeleri et al., 2018; Vasconcelos et al., 2020; Wanderley et al., 2013). A more consistent decrease in IL-6 was found in functional exercise, as well as a combination of aerobic and resistance exercise (Lima et al., 2015; Vasconcelos et al., 2020; Wanderley et al., 2013), while some pure resistance training protocols, especially with longer intervention durations, showed no significant change (Hangelbroek et al., 2018). In addition, one study reported an increase in IL-6 immediately after a workout session as an acute response (Phillips et al., 2012). However, the chronic effects of exercise tended to be stable or decreased (Tomeleri et al., 2016; Tomeleri et al., 2018).

b. TNF-α

Five studies (62.5%) of the 8 analyzed studies reported a significant decrease in TNF-α levels after exercise interventions (Lima et al., 2015; Phillips et al., 2012; Tomeleri et al., 2016;

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Tomeleri et al., 2018; Vasconcelos et al. 2020). A more consistent decrease in TNF-α was found in pure resistance training, as well as a combination of resistance and aerobic exercise (Phillips et al., 2012). However, some interventions, such as kettlebell training and long-duration resistance training, did not show significant changes in TNF-α levels (Chen et al., 2018; Hangelbroek et al., 2018).

Patterns of Effectiveness based on Types of Exercise

Patterns of exercise effectiveness suggest that pure resistance training more consistently lowers TNF-α than IL-6 (Phillips et al., 2012; Tomeleri et al., 2016, 2018). Functional exercise shows high effectiveness against both biomarkers, although evidence is still limited (Vasconcelos et al., 2020). Aerobic exercise is more effective at lowering IL-6, while the combination of resistance and aerobic exercise is effective at lowering TNF-α, but does not always have a significant impact on IL-6 (Lima et al., 2015; Wanderley et al., 2013). In general, the most frequent exercise protocols showing effective anti-inflammatory effects lasted 8–24 weeks, with a frequency of 2–3 sessions per week and an intensity of 60–80% of one repetition maximum (1RM).

Heterogeneity and Limitations

The heterogeneity of exercise protocols, participant characteristics, and biomarker measurement methods affected the consistency of results between studies, with lower effectiveness in the frail/pre-frail older adult population compared to the older adults with obesity or sarcopenia. The dominance of female participants, small sample size, and short duration of follow-up limit the generalization of findings and the evaluation of long-term effects.

Summary of Key Findings

Resistance training showed consistent potential in lowering TNF-α and IL-6 levels at lower levels in the older adults. The effectiveness of the intervention was influenced by the type of exercise, duration, intensity, and characteristics of the participants. Therefore, follow-up research with more standardized protocols and longer duration of interventions is still needed to strengthen the existing evidence.

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Table 3. Descriptive Characteristics of The Selected Study

	Vasconcelos et al. (2020)	Lima et al. (2015)	Phillips et al. (2012)	Chen et al. (2018)	Hangelbroek et al. (2018)	Tomeleri et al. (2016)	Tomeleri et al. (2018)	Wanderley et al. (2013)
Age	60–75	60–75 (Hypertension)	60–70 (Obese Woman PM)	65–75 (Sarcopenia)	> 65 (Frail & Pre-Frail)	≥ 60 (Obesities)	≥ 60 (Average of 70.6)	> 60
Intervention (Group)	Functional (FT) vs. Traditional (TT) vs. Control (CG)	Aerobic (AG), Resistance + Aerobic (RAG), Control (CG)	Resistance Training (RT) vs. Social Interaction (SI/CON)	Kettlebell Training (KT) vs. Control (CON)	Progressive Resistance Exercise Training (RT)	Resistance Training (RT) vs. Control (CG)	Resistance Training (RT) vs. Control (CG)	Training (AT), Resistance Training (RT), Control
Duration & Frequency	24 weeks, 3x/week	10 weeks, 3x/week	12 weeks, 3x/week	8 weeks, 2x/week	24 weeks, 2x/week	8 weeks, 3x/week	12 weeks, 3x/week	8 months, 3x/week
Muscle Strength (Results)	Significant improvement in Muscle Power (FT & TT).	RAG included resistance training, focusing on inflammation/BMI.	RT: increased strength 44%.	KT significantly increased grip strength and back strength, with a retention effect.	RT increased strength (1RM Leg Press/Extension).	RT showed an increase in total strength (1RM).	RT caused an increase in SMM and was positively correlated with changes in Phase Angle (PhA).	AT increased functional capacity (6MWD).
Outcome Indicators (Inflammatory IL-6 & TNF-α)	TNF-α ↓ (FT & TT). IL-6 ↓ only on FT.	IL-6 ↓ (AG vs. CG). TNF-α ↓ (RAG vs. CG).	TNF-α ↓ (29%). Plasma IL-6 Acute ↑ after training.	No significant changes to IL-6 or TNF-α. However, hs-CRP ↓ was significant.	RT did not affect the circulating levels of IL-6 or TNF-α.	TG showed significantly lower values for IL-6 and TNF-α compared to CG.	TG showed a significant decline in TNF-α (-15.2%) and IL-6 (-17.9%); IL-10 increased.	AT reduced hs-CRP and IL-6 (-43.5%) in high-risk individuals. Control experienced an increased TNF-α.

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Table 4. Summary of Key Findings

Categories of Quality	Author (Year)	Score PEDro	Types of Interventions	Duration	IL-6	TNF-α	Main Notes
Good	Tomeleri et al. (2016)	7	Resistance Training	8 weeks	↓	↓	Significant decline, correlation with strength
	Tomeleri et al. (2018)	7	Resistance Training	12 weeks	↓	↓	Significant decrease, correlation with Phase Angle
	Vasconcelos et al. (2020)	8	Functional vs Traditional	24 weeks	↓	↓	FT was most effective for IL-6 and TNF-α.
Fair	Lima et al. (2015)	5	Aerobic vs Combination	10 weeks	↓	↓	Effective combination for TNF-α
	Phillips et al. (2012)	5	Resistance Training	12 weeks	↑	↓	IL-6 rose acutely, TNF-α dropped
	Chen et al. (2018)	4	Kettlebell Training	8 weeks	-	↔	No significant changes
	Hangelbroek et al. (2018)	5	Progressive Resistance	24 weeks	↔	↔	No significant changes
	Wanderley et al. (2013)	4	Aerobic vs Resistance	8 months	↓	↔	Effective aerobics for CRP

Description: ↓ = significant decrease ↑ = significant increase ↔ = no significant change * = not measured

DISCUSSION

This systematic review shows that resistance training has a potential anti-inflammatory effect in older adults, with a more consistent decrease in TNF-α levels than IL-6. Of the eight randomized controlled trials analyzed, 62.5% of studies reported significant reductions in TNF-α, while reductions in IL-6 were reported in 50% of studies (Lima et al., 2015; Phillips et al., 2012; Tomeleri et al., 2016, 2018). Pure resistance training tends to be more effective in lowering TNF-α, while functional training shows promising results against both biomarkers (Lima et al., 2015; Tomeleri et al., 2016; Tomeleri et al., 2018; Vasconcelos et al., 2020; Wanderley et al., 2013). The exercise protocol that most often showed positive results lasted 8–24 weeks and performed 2–3 times per week with moderate to high intensity (60–80% 1RM).

The difference in response between IL-6 and TNF-α can be explained by different physiological roles. IL-6 has a dual function as a pro-inflammatory cytokine and as a myokine that is released during muscle contraction (Pedersen and Febbraio, 2012). An acute increase in IL-6 after exercise reflects a physiological metabolic response (Tomeleri et al., 2018). In the long term, resistance training can stabilize or decrease IL-6, along with improved muscle quality and metabolic efficiency (Zhao et al., 2023). In contrast, TNF-α is a more stable marker of chronic inflammation and is directly related to muscle catabolism. A more consistent decrease in TNF-α suggests that resistance exercise effectively lowers systemic inflammatory burden through increased muscle mass, improved insulin sensitivity, and decreased production of pro-inflammatory cytokines from adipose tissue, as well as an increase in anti-inflammatory cytokines such as IL-10 (Magni, Arnaoutis, and Panagiotakos, 2025).

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The results of this study are in line with previous reviews and meta-analyses that reported that resistance exercise was effective in lowering TNF-α in the older adult population (Monteiro-Junior et al., 2018), although with large variations between studies. In contrast to most previous reviews that focused on aerobic exercise or combination exercise, this review confirms that resistance training as the main intervention has specific anti-inflammatory effects, particularly against TNF-α (Leal, Lopes, and Batista, 2018). Aerobic exercise is reported to be more consistent in lowering IL-6 (Guo et al., 2024; Zheng et al., 2019), while combination exercise and functional exercise have the potential to provide synergistic effects, although evidence is still limited (Khalafi et al. 2023).

The main strength of this study is the use of a systematic review design that only includes controlled randomized trials and methodological quality assessment using the PEDro scale. The focus on resistance training as the primary intervention provides clarity in the interpretation of its effects on inflammatory biomarkers. However, this study has several limitations, including the heterogeneity of the training protocol, the characteristics of the participants, and the biomarker measurement method, which inhibit the meta-analysis. The relatively small sample size, short follow-up duration, and the dominance of female participants also limited the generalization of the findings. Confounding factors such as diet, sleep quality, and drug use had not been consistently controlled.

These findings support resistance training as a promising non-pharmacological approach to reducing age-related chronic inflammation, particularly through a decrease in TNF-α. In the context of physical education and exercise, structured resistance training can be integrated into the physical activity programs of older adults, both in adaptive physical education, community fitness programs, and promotive-preventive interventions to support healthy aging. Further research needs to use a randomized controlled trial design with larger sample sizes, longer duration of intervention and follow-up, and more standardized training protocols. Future studies also need to consider differences in responses by gender, early health status, and the interaction of exercise with lifestyle factors. Exploration of functional exercise and multimodal exercise programs is also needed to optimize inflammatory management strategies in older adults.

CONCLUSION

Resistance training has the potential to lower inflammatory biomarkers in older adults, especially TNF-α, although the effects on IL-6 still vary. The heterogeneity of the training protocol and the characteristics of the participants limited the generalization of the findings. Further research with a more standardized design, longer duration of interventions, and control of lifestyle factors is needed to strengthen the scientific evidence in the context of physical education and exercise for older adults.

AUTHORS' NOTE

The authors declare that there is no conflict of interest regarding the publication of this article. The authors confirmed that the paper was free of plagiarism.

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